

LETTERS TO THE EDITOR

The rostrocaudal gradient for somatosensory perception in the human postcentral gyrus

Anatomical organisation of the primate postcentral gyrus has been described in terms of several different cytoarchitectures.^{1,2} Powell and Mountcastle stated that the area 3 was a typical koniocortex with granular cells, whereas in areas 1 and 2 the morphological characteristics changed gradually to the homotypical parietal association cortex in the monkey *Macaca mulatta*.¹ Iwamura *et al* reported the physiological correlates on the anatomical rostrocaudal axis in monkeys.² The ratio of skin neurons to total neurons was the largest in area 3b and decreased gradually toward the caudal part of the postcentral gyrus.² Specific types of stimulation such as rubbing of the skin in certain directions were effective in activating some of the caudal part of the postcentral gyrus. The anatomical and physiological data in the primate lead to the reasonable hypothesis that there is a rostrocaudal functional gradient within the postcentral gyrus. This notion may explain why a lesion in the postcentral gyrus causes varied sensory disturbance in various people.

A 49 year old right handed man suddenly developed dysaesthesia in the right hand. This recovered gradually, but 1 month later he still had an impaired tactile recognition for objects. His voluntary movements were skillful. Deep tendon reflex was slightly exaggerated in his right arm. Babinski's sign was absent. His language was normal. Brain MRI on the 35th day after the onset showed a laminar necrosis on the caudal edge of the lateral portion of the left postcentral gyrus (figure).

Somaesthetic assessment was done during the 21-28th days of the illness.

Elementary somatosensory functions were assessed, including light touch (long fibre cotton), pain (pinprick), thermal sensation (cold and hot water), joint position sense (tested by the ability of the patient to identify flexion or extension of fingers with closed eyes), and vibration sense (128-Hz tuning fork).

Intermediate somatosensory tasks were carried out. For two point discrimination, the examiner placed a pair of plastic needles of a slide caliper on the index finger pad of the patient, who had his eyes closed, and asked him to answer the number of touched needles, "one" or "two". For tactile localisation the examiner touched a point on the right or left hand of the patient, who had his eyes closed, with a brush, then asked him to indicate the point by touching the place with the first finger of the counter hand. For weight perception, the patients were asked to arrange the stimuli in a correct order of the weight with either the left or right hand. The stimuli were six metal plates of equal size,

shape, and texture weighing 50, 60, 70, 80, 90, and 100 g. For texture perception, we prepared six wooden plates of an identical size and shape, on which one of six different textures (sandpaper, felt, wood, wool, fine grain, synthetic rubber) were mounted. The patient palpated one texture by either hand with his eyes closed. Then he was asked to select tactually a correct one among the six textures. For shape perception (three dimensional figures) the patient palpated one of the five wooden objects (cylinder, cube, sphere, prism, and cone) with his eyes closed. Then he was asked to explain the shape verbally. For extinction, the examiner delivered light and brief tactile stimuli, using the tips of the index fingers, to the dorsal surface of left, right, or both hands of the patient.

For tactile object recognition, the 15 objects that are used in the naming list of the Western aphasia battery test were presented to either hand. For naming of objects, the patient was asked to name a single manipulated object. In matching of objects, the patient first grasps a single object among a selection of five objects, and then he was asked to select the correct object among the five.

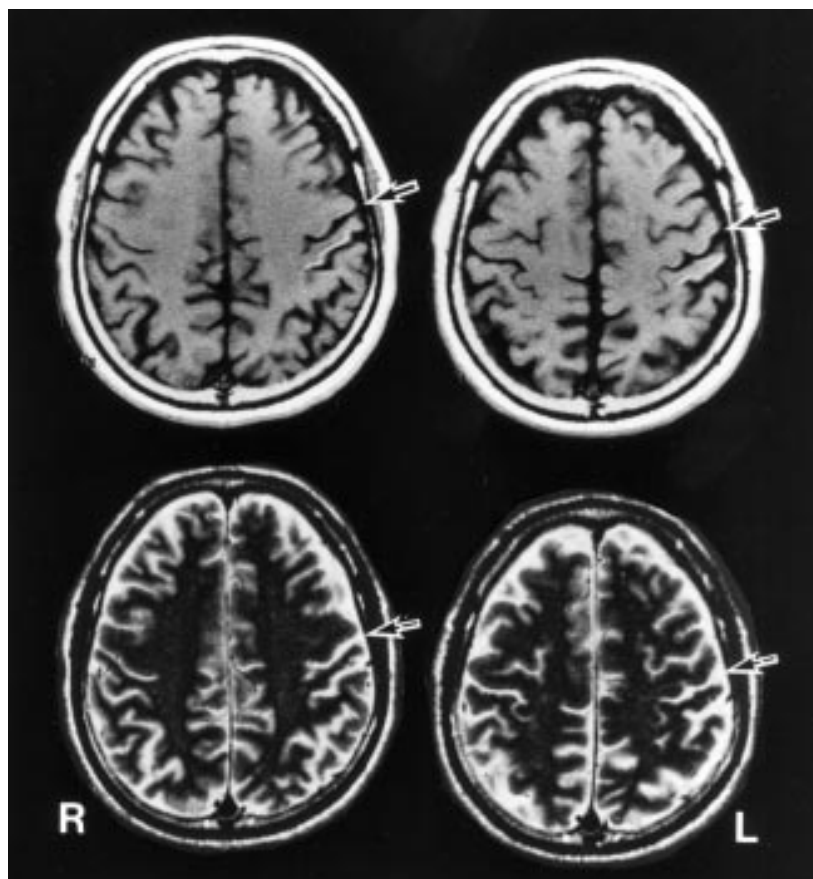
In elementary sensory function, the test for light touch, pain, thermal sensation, joint position sense, and vibration sense demonstrated no abnormalities for both hands. The results of intermediate sensory tests showed that in all tests, except for shape perception, we could detect no disturbance in both hands. He could not discriminate the shape with his right hand. The correct responses were 5/5 with the left hand and 0/5 with his right hand. The correct responses in the tactile naming test were 2/15 for the right hand and 15/15 for the left hand. The correct responses of the tactile-tactile matching test was 4/15 with his right hand and 15/15 with his left hand. So the abilities of tactile recognition and tactile-tactile matching were disturbed with the right hand.

According to Delay, disturbances of the tactile process in the cortex are classified into at least three types.³ Ahylognosia is a disturbance in the ability to discriminate materials. Amorphognosia is a disturbance in the differentiation of forms. Tactile agnosia is the inability to recognise the identity of objects in the absence of ahylognosia and amorphognosia. In Delay's terms, our patient showed amorphognosia but not tactile agnosia. Iwamura and Tanaka suggested that the hand region of area 2 in the rhesus monkey is concerned with the tactile perception of the discrimination of certain object forms.⁴ The lesion localised at the equivalent cortical region. This region thus may be critical for the tactile discrimination for shape.

Rich intrinsic corticocortical connections are demonstrated within the rhesus monkey's postcentral gyrus, starting from Brodmann area 3b and projecting to areas 1 and 2.⁵ This corticocortical connection may be a main route of inputs to area 2. This suggests that within the postcentral gyrus somatosensory information is processed from primary sense reception to integrating and more associating stages. The results from our patient are compatible with the notion that in the caudal portion of the human postcentral gyrus the more complex process such as shape perception is processed.

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Brain MRI of the patient. Transaxial T1 weighted (above) and T2 weighted images (below) are shown. The T1 weighted image disclosed a high intensity lesion distributed laminarly in the caudal edge of the left postcentral gyrus (Brodmann 1-2). Arrows indicate the left central sulcus.

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Isolated spastic paraparesis leading to diagnosis of Friedreich's ataxia

Friedreich's ataxia is the most common hereditary ataxia. This neurological disorder was initially defined by the association of ataxia, cerebellar syndrome, and pyramidal signs. Atypical forms are increasingly recognised. The gene was mapped to 9q13-q21.1 in 1988 and identified in 1996. We report on a patient with a spastic paraparesis, of which molecular analysis confirmed the diagnosis of Friedreich's ataxia.

A 39 year old woman without any past condition presented with difficulty in walking since the age of 20. Neurological examination showed a spastic paraparesis, with tetrapyramidal signs, including generalised brisk reflexes, bilateral Babinski's signs, and clonus at the knees and ankles. Spasticity only concerned the lower limbs and spared the arms. Spastic paraparesis resulted in impaired walking at the time of the examination. No other neurological abnormalities were found; notably, proprioception and vibration sense, and cerebellar function were normal. No sensory symptoms were noted. No skeletal deformities were found. All hematological investigations (including lactate and pyruvate concentrations, cholesterol, apolipoproteinemia, Vitamin E, very long chain fat acid concentrations, arylsulphatase, and hexosaminidase activities) were normal. Electromyography, sensory and motor nerve conduction studies in the upper and lower limbs, including sural nerve action potentials (right sural nerve action potential 7 μ V, normal >6 μ V; left sural nerve action potential 8 μ V, normal >6 μ V) were normal. Cardiological tests (electrocardiography, transthoracic echocardiography) were normal. Cerebral and spinal resonance MRI were normal. No familial condition was found, except the sister who presented the same symptoms. No mutations involved in mitochondriopathies were found

(3243tRNA^{Leu}, 8344tRNA^{Lys}, nt 8993). The molecular analysis of the gene coding for Friedreich's ataxia was performed by Southern blotting from DNA extracted from peripheral blood and showed two abnormal expansions of 2.5 kb and 3.1 kb on the chromosome 9q13-q21.1 (Dr M Schmitt, CHRU de Strasbourg, France). These expansions correspond to 830 and 1030 repeats. Diagnosis of Friedreich's ataxia identified by an isolated paraparesis was definitely retained.

Friedreich's ataxia, an autosomal recessive disorder, is one of the most common hereditary ataxias. The frequency of the gene is close to 1/90 in the general population and the prevalence of the disease is estimated to be 1/50 000. Diagnosis is classically based on the association of recessive inheritance, onset before the age of 25, progressive ataxia of the four limbs, loss of deep tendon reflexes, pyramidal signs, cerebellar dysarthria, distal loss of position and vibration sense, and electrophysiological evidence of axonal neuropathy.¹ Association of pes cavus, scoliosis, cardiomyopathy, hearing loss, diabetes, and retinal disease are inconstantly seen. By contrast, atypical clinical symptoms are increasingly encountered—for example, late onset, brisk reflexes, spasticity, and slow progression of the disease,² and idiopathic ataxia.³ Friedreich's ataxia is a genetically homogeneous condition. The frataxin gene was mapped to 9q13-q21.1 in 1988,⁴ and identified in 1996.⁵ The mutations are most often GAA expansions located in the first intron.⁵⁻⁷ Normal alleles range from 6 to 36 GAA repeats, whereas pathological alleles range from 90 to 1300 repeats. Ninety six per cent of patients are homozygous for GAA trinucleotide repeat expansions in the first intron of the frataxin gene. The remaining patients are compound heterozygotes for a GAA expansion and point mutations (missense, nonsense, and splice site mutations).^{5,7} Frataxin, the protein encoded by the gene, is a protein associated with the inner mitochondrial membrane.⁸ It is thought to regulate the flux of iron in or out the mitochondria. Identification of the mutated gene allowed the correlation of certain phenotypes with genotypes. Larger expansions of the GAA repeats are correlated with an earlier age of onset, a faster progression of the disease, and additional clinical manifestations such as cardiomyopathy, pes cavus, scoliosis, and extensor plantar responses.⁶ The length of the expansion explains 50% of the variability of age at onset only. Other factors are certainly involved in the phenotype variability. We note that the correlations were established from expansions measured in lymphocytic DNA. We cannot exclude the possibility of somatic mutations. Thus, the length of expansion in affected tissues would be different from the length found in lymphocytes. Some punctual mutations (D122Y, G130V) are correlated with a mild phenotype.⁷ Previous reports have noted that patients with Friedreich's ataxia could present with spasticity, usually associated with other neurological signs.⁹ Our report of isolated paraparesis confirmed again that the phenotypic range of Friedreich's ataxia is much broader than previously considered.^{3,6} In addition, the spastic paraparesis presented by our patient could be related to the cases of mitochondriopathies presenting with spastic paraplegia. Similar clinical symptoms in these two diseases can be an additional argu-

ment for the implication of frataxin in mitochondrial function.

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Marked increase of interleukin-6 in injured human nerves and dorsal root ganglia

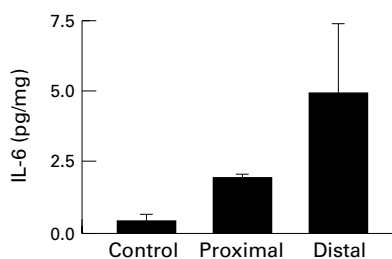
Nerve injury, particularly of the brachial plexus, may result in lifelong disability and chronic pain, despite technically excellent reconstructive surgery. Studies of molecular changes in injured nerves may identify new treatments to enhance the success of nerve repair, such as with recombinant human neurotrophic factors. Interleukin-6 (IL-6) is a member of the neurotrophic cytokine family that includes ciliary neurotrophic factor (CNTF), leukaemia inhibitory factor (LIF), and oncostatin M. As there is increasing evidence of a neurotrophic role for IL-6 in animal models of nerve injury and inflammation,^{1,2} we have studied, for the first time in humans, IL-6 protein in injured and control peripheral nerve and dorsal root ganglia, using specific immunoassay, immunocytochemistry, and western blotting. We report a most remarkable increase of IL-6 concentrations in acutely avulsed dorsal root ganglia and injured nerves.

Proximal and distal injured nerve segments were obtained from six adult patients with traction brachial plexus injury, ranging from 2 weeks to 10 weeks after trauma. Injured dorsal root ganglia were collected from seven adult patients with brachial spinal root avulsion injuries (central axotomy), ranging from 3 days to 15 months after trauma. Tissue removal was a necessary part of the surgical repair procedure; in all cases

informed consent was obtained for tissue collection, and the study had ethics committee approval. Control dorsal root ganglia were obtained from four subjects and segments of normal nerve from five subjects at postmortem, with a mean delay of 36 hours after death; all died from myocardial causes. Tissue extracts prepared as previously described^{3,4} were analysed for IL-6 using an enzyme immunoassay (Peline CompactTM, Eurogenetics, UK Ltd, Middlesex, UK) with recombinant human IL-6 standard calibrated against the World Health Organisation (WHO) First International Standard 89/548. For immunohistochemistry, frozen sections (8 µm) were fixed in 4% paraformaldehyde in phosphate buffered saline for 30 minutes. Sections were incubated with monoclonal antibodies to IL-6 (CLB.IL-6/7 20 µg/ml, diluted 1:400; gift from K Nordlind, Sweden, or ref No 1618-01, Genzyme, USA) and immunoreactivity to IL-6 visualised using a standard immunoperoxidase method (ABC; Vector Labs, UK) with nickel enhancement as described elsewhere.^{3,4} Specific immunoreactivity was extinguished by a concentration of rhIL-6 (ImmunoKontakt, Frankfurt, ref 111-40-136) in the range 0.01–0.1 µg/ml. For western blotting, tissue extracts were separated by gel electrophoresis on 15% acrylamide gels and then electrophoretically transferred to nitrocellulose membranes (Hybond Super, Amersham) using a semidry transblotter. Strips were blocked in a solution of 5% non-fat milk in phosphate buffered saline (PBS) containing 0.05% Tween-20 for 1 hour and then probed with CLB.IL-6/7 (with or without IL-6 peptide, 20 µl) at a final titre of 1:1000, for 2 hours. The strips were then incubated with anti-rabbit HRP (Sigma) at 1:10,000 dilution for a further 30 minutes. Bands were then visualised on x ray film after treatment with ECL reagents (Amersham).

Concentrations of IL-6 were increased in injured nerves (figure). The increase was greater in nerve segments distal to injury, but IL-6 concentrations in both proximal and distal segments were both significantly increased compared with controls ($p < 0.01$, Mann-Whitney test). Concentrations of IL-6 were greatly raised in two avulsed dorsal root ganglia obtained 3 and 4 days after injury (354 pg/mg and 128 pg/mg). At longer operative delays after injury, IL-6 concentrations in avulsed dorsal root ganglia approached the range of values obtained for postmortem controls (4.9 (SD 2.9) pg/mg for operative delays from 1 week to 15 months, and 0.2 (SD 0.06) pg/mg for controls). Western blotting showed the presence of an expected strong 29 kDa band in detergent extracts of injured nerve, which was abolished in the presence of excess synthetic IL-6. Immunohistochemical studies with both antibodies demonstrated IL-6 staining within the soma of avulsed dorsal root ganglion neurons of all sizes, particularly of small size. Immunostaining of postmortem ganglia seemed similar in pattern, but was generally weaker. Interleukin-6 immunoreactivity was also seen in nerve-like structures within the dorsal root ganglia and distal injured nerve segments.

The pattern of changes of IL-6 in injured nerves and dorsal root ganglia differs from that seen for other neurotrophic factors, such as nerve growth factor (NGF) and glial-derived neurotrophic factor (GDNF).^{3,4} Concentrations of IL-6 were usually higher in distal nerve segments when compared with those proximal to the site of injury: this seems



IL-6 immunoreactivity in human nerve tissues. Assay concentrations of IL-6 in extracts of human nerve, comparing segments proximal and distal to injury with control postmortem nerve.

to result from IL-6 synthesis in Schwann cells in Wallerian degeneration, as shown by immunostaining, and previous animal model studies.² Interleukin-6 and its receptor have been shown to be required for normal nerve regeneration in animal models, which may be enhanced with exogenous IL-6.¹ The injured nerves presumably take up IL-6 synthesised in the Schwann cells, and transport it proximally, which accounts for the higher IL-6 concentrations in proximal segments of injured nerves in comparison with controls. Anterogradely transported IL-6, if released in the spinal cord, may play a part in pain processing, for which there is some evidence from animal models. In this study, the most remarkable finding was the very high concentration of IL-6 in extracts of the acutely avulsed dorsal root ganglia, with much smaller increases at later times after injury. The acute increase of IL-6 could originate from sensory cell bodies themselves, as has been shown with IL-6 mRNA in situ hybridisation studies in rat sensory ganglia after peripheral nerve injury,⁵ or from inflammatory cells. This increase may have autocrine/paracrine effects, which may aid cell survival, or have a role in sensory or sympathetic sprouting.

We conclude that IL-6 is a significant factor in the events after nerve injury in humans, particularly in sensory neurons. The potential therapeutic role in nerve repair for recombinant human IL-6, and agents that modulate its action, deserves further investigation.

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Crossed face apraxia

Apraxia refers to the disorder of movement planning and execution that cannot be accounted for by motor or sensory deficits nor by other cognitive impairments. The term apraxia encompasses several different deficits, including "face apraxia", which defines the impairment of movements performed within the district of the cranial nerves. Group studies have shown that face apraxia results from lesions of the left hemisphere.¹ However, a few cases can be gleaned from the literature of patients whose face apraxia followed lesions in their right hemisphere and was mentioned in fleeting comments.^{2–4}

Face apraxia has generally been equated to oral apraxia and tests aimed at assessing it only comprise items exploring skilled movements of the lips, cheeks, and tongue. However, several early authors reported on patients with face apraxia also showing movement deficits of the eyes and eyebrows.⁵ Some anecdotal evidence of upper face apraxia is also reported in more recent investigations.⁶ We report on a patient, who, 2 years after a right hemispheric lesion, showed severe face apraxia for movements of both the lower and the upper parts of the face. A 55 year old artist with 17 years of education had an ischaemic stroke in August 1997. A series of CT and MR scans showed a right frontoparietal insular hypodensity also encroaching on the anterior region of the right internal capsule and of the right deep nuclei, sparing the mesial and the anterior part of the parietal lobe. He had always been right handed, scored 100% right handed on both the Edinburgh handedness questionnaire⁷ and the 12 question handedness inventory.⁸ He also denied familiarity for left handedness. We examined the patient in October 1999, 5 months after the end of his rehabilitation therapy and more than 2 years after his stroke. He still showed a severe left paresis, hemianopia, and a deficit of the lower facial nerve. No further deficits of the cranial nerves were seen. In particular, spontaneous movements of the oculomotor nerves were normal. The patient did not show general cognitive impairment: his scores on intelligence tests were well within the normal range. At the time of our assessment he did not show clear evidence of visuospatial neglect which was mentioned in the clinical notes at onset. He performed flawlessly tasks assessing the ability to search for particular targets, in reading, or in line bisecting, although he omitted a few left details in copying complex geometrical drawings. During neurological examination the patient proved unable to close his eyes on verbal command. He failed even when the examiner showed him how to do it. He was therefore submitted to a battery of tests assessing apraxia including the upper and lower face apraxia test.⁹ The nine upper and 29 lower items of the test were performed first on imitation and then, considering the possibility that the patient could have some difficulty in perception, on verbal command. On imitation, the patient scored 2/45 and 320.25/435 (adjusted scores) on the upper and lower face

sections of the test respectively, both well below the inner tolerance limit cut off scores (38.43/45; 400.04/435). On command he failed all items of the upper face test and he failed the same items of the lower face test which he failed on imitation.

His errors were perseveration of the previous item or substitutions with another movement—for instance, when asked to make a clip-clop noise with his tongue, he showed his teeth, then made his teeth chatter. Similarly, asked to close his eyes, he said “yes” at first, then he opened his mouth, then he tried to show his tongue. He was unable to close either his right or his left eye, to look leftward or rightward keeping his head motionless, or to wrinkle his forehead or his nose.

The patient's face apraxia could not be due to motor impersistence because he was not required to hold a position for a given time.¹⁰ Moreover, the fact that his face apraxia was long lasting excludes the possibility that upper face apraxia has to be drawn back to diaschisis or other similar phenomena. Finally, neglect had recovered at the time of testing and there was no cognitive deterioration to account for the presence of this symptom.

Ideomotor apraxia was also assessed by means of a 24 item test.¹¹ His score with the right arm and hand was normal (64/72, cut off score=53). The patient was not aphasic; his language was emitted with a normal prosody, was well articulated, informative, and without qualitatively aphasic errors.

This case points to a possible role that the right hemisphere might have in normal facial praxis, both for the lower and upper face areas, in some people. Moreover, it confirms the dissociation between face apraxia and aphasia, as well as between limb and face apraxia.

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A case of Bickerstaff's brainstem encephalitis mimicking tetanus

Bickerstaff's brainstem encephalitis is characterised by acute ophthalmoplegia and ataxia with progressive consciousness disturbance.¹ Although Bickerstaff described rigidity in the recovery phase,¹ rigidity in the clinical course of Bickerstaff's brainstem encephalitis has rarely been reported.² We encountered a case in which the initial diagnosis was tetanus, because of the progression of severe rigidity and risus sardonius, but which turned out to be Bickerstaff's brainstem encephalitis owing to the presence of anti-GQ1b IgG antibody.

A 23 year old man who had had no prior apparent infectious episode began to show dysaesthesia, clumsiness, and slight weakness of all limbs (day 1). Due to rapid exacerbation of these symptoms he was admitted to a hospital the next day. On day 3, he became irritable because of increased anxiety, although he was alert and completely oriented. He was transferred to another hospital for further treatment. There he required assistance in walking because of new severe rigidity in all his limbs. Oral haloperidol (maximum dose 20 mg/day) was given for 10 days to reduce his anxiety, but his symptoms did not lessen. Treatment with intravenous methylprednisolone (1000 mg/day) from day 14 to 16, as well as acyclovir (1500 mg/day) given intravenously, failed to ameliorate his symptoms. On day 17, he was transferred to our hospital for further evaluation and treatment.

Physical examination on day 17 showed a body temperature of 37.0°C, blood pressure 130/80 mm Hg, pulse rate 100 beats/min, respiratory rate 12/min, and severe hyperhidrosis. Neurological examination showed that he was alert and well oriented. The pupils were isocoric and round but mydriatic. Light reflexes were prompt. Bilateral blepharoptosis was present. Extraocular movement was completely inhibited vertically and horizontally. Restriction of mouth opening and dysarthria similar to risus sardonius were caused by increased tonus of the masseter muscles. Neither tongue atrophy nor fasciculation was present. Tests for muscle strength and coordination could not be made due to severe rigidity of the neck, trunk, and limbs. Deep tendon reflexes were absent, probably secondary to the rigidity. The Babinski response was negative bilaterally. Voluntary movements were markedly slow, and sitting balance was poor. Opisthotonus was not present. No abnormality was found in the sensory examination. Because of Forley catheter placement due to the patient's severe general condition, we did not evaluate his bladder function.

White blood cell count was 13 320/mm³ (84% neutrophils), but the erythrocyte sedimentation rate and C reactive protein concentration were normal. Protein in CSF was 144 mg/dl with normal cellularity. No oligoclonal IgG bands were detected in the CSF. Magnetic resonance imaging detected no abnormalities in the brain stem. An EEG was normal. Motor nerve conduction velocities and compound muscle action potentials measured in the right median, ulnar, and posterior tibialis nerves were normal, but no

F waves were evoked. Antidromic sensory nerve velocity in the right median nerve was normal, but no sensory activation potentials were evoked in the right ulnar and posterior tibial nerves.

Based on his clinical course and the physical examination, the tentative diagnosis was general tetanus. On day 18, intravenous piperacillin sodium (4000 mg/day) and oral dantrolene sodium (25-50 mg/day) were started. On day 19, 4500 IU human anti-tetanus immunoglobulin (Tetanobulin®, Yoshitomi, Tokyo, Japan) was infused. On day 20, his bilateral blepharoptosis and rigidity of the limbs began to lessen. Subsequently his symptoms and signs improved dramatically. On day 24 he could turn himself over in bed. On day 25 ophthalmoplegia was ameliorated with slight limitation of lateral gaze. On day 26 he could sit independently. On day 32 he could stand without assistance, and on day 37 he could walk independently. During the recovery phase, no ataxia was seen. He has not had a relapse for 2 years and 6 months.

After his recovery, we evaluated the anti-ganglioside antibodies and antitetanus antibody activity in his serum. An enzyme linked immunosorbent assay³ showed that serum IgG on day 19 had high (4000) anti-GQ1b antibody titre. The IgG antibodies did not react with GM1, GM2, GD1a, GalNAC-GD1a, GD1b, or GT1b. Thin layer chromatography with immunostaining confirmed that the patient's IgG bound strongly to GQ1b, but not to GM1, GD1a, GD1b, or GT1b. No anti-GQ1b IgG antibody was detectable (titre<500) 2 years and 6 months after the onset of neurological symptoms. By contrast, the neutralising antitetanus antibody activity in the serum on day 17 was 0.41-0.75 IU/ml, sufficient for protection against tetanus infection.⁴

Serum anti-GQ1b IgG antibodies have been found in patients with Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoparesis, acute ophthalmoparesis, and Bickerstaff's brainstem encephalitis.⁵ Albumino-cytological dissociation in CSF and poor F wave response of the examined nerve are compatible with Miller Fisher or Guillain-Barré syndrome. The clinical findings, most characteristic of this patient, however, were severe rigidity of the face, neck, trunk, and limbs, which has not been described in Miller Fisher syndrome, Guillain-Barré syndrome, or acute ophthalmoparesis. The extrapyramidal side effect of haloperidol was unlikely because rigidity was present before the drug was administered. Bickerstaff reported the development of parkinsonism, including rigidity, within 2-4 weeks of onset and during the recovery phase in Bickerstaff's brainstem encephalitis, with the exception of a fatal case in which parkinsonism developed before maximal disability.¹ Our patient showed rigidity from the beginning. Although an overlap of Guillain-Barré syndrome could not be excluded,³ our diagnosis was Bickerstaff's brainstem encephalitis, because the patient's case was close to the exceptional one reported by Bickerstaff. Antitetanus immunoglobulin is comprised of high dose polyclonal IgGs to tetanus toxin and other types of IgGs and IgMs, and it may have had an effect similar to that of intravenous immunoglobulin in our patient. His dramatic recovery immediately after antitetanus immunoglobulin administration could not be explained as part of a natural course. Although the mechanism for the early appearance of rigidity in our

reported case is not clear, Bickerstaff's brainstem encephalitis should be considered the differential diagnosis when rigidity, such as tetanus, is present.

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Lysozyme in ventriculitis: a marker for diagnosis and disease progression

The development of a hydrocephalus as a typical complication after subarachnoid haemorrhage often requires implantation of a catheter for drainage of ventricular fluid. Because this is an open system it carries a risk of development of bacterial ventriculitis by contamination. This potentially life threatening or neurologically disabling disease can be diagnosed by microbiological tests on the CSF. However, microbiological examination is often not possible or shows pathological results only after a delay, probably because of antibiotic prophylaxis. Standard CSF indices are difficult to interpret, because subarachnoid haemorrhage leads to an irritation syndrome in the CSF, which can imitate infection.

Lysozyme is a basic polypeptide of 129 amino acids weighing 15 kDa, which is found in neutrophilic granulocytes or monocytes, and is released from cytoplasmic and azurophilic granules.¹ It is capable of degrading bacterial proteoglycans.² Lysozyme shows significantly higher concentrations in CSF in bacterial meningitis in comparison with abacterial meningitis, whereas in other diseases of the CNS much lower concentrations are found.^{3,4}

We retrospectively documented the results from 146 patients who underwent external ventricular drainage after subarachnoid haemorrhage. As well as documenting the frequency and timing of infection, the medical notes were inspected for risk factors of infection.

In 64 patients (15 with microbiologically confirmed ventriculitis, and 49 with no

evidence of ventriculitis) the following measurements were compared: serial CSF cytology; total protein; albumin; IgM, IgA, IgG; plasma/CSF ratio of albumin, IgM, IgA, IgG; locally produced fraction of IgM, IgA, IgG and CSF oligoclonal IgG, lactate, and glucose.

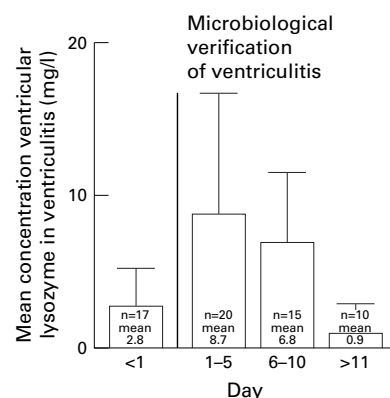
For further analysis, 61 CSF samples were available from 14 patients with microbiologically confirmed ventriculitis. As a control, we used one sample from each of 31 patients in whom no evidence of ventriculitis was found. Immediately after these CSF samples had been collected for clinical tests, the remainder of the samples had been frozen at -80°C. These CSF samples were investigated to measure their lysozyme concentrations by radial immunodiffusion. The sample is transferred to circular wells in an agarose gel; the antigen then diffuses radially from the sample into the gel, which contains the corresponding antibody. After an incubation period (18 hours) the antigen concentration can be read from a reference table ("The binding site", Birmingham, UK).

For statistical analysis we used the χ^2 test, the Wilcoxon matched pairs test, and a Kaplan-Meier survival analysis. A p value <0.05 was considered to be statistically significant.

Fifteen of 146 patients (10.3%) developed a microbiologically established ventriculitis, confirmed by detection of *Pseudomonas aeruginosa* (one case), *Staphylococcus epidermidis* (12 cases), gram negative rod cells (one case), and enterococci (two cases). The period of drainage was 3-39 days (mean 10 days). Infection rate was 3.5% (5/146) within the 1st week, 5.3% (4/77) within the 2nd week, and 15.4% (6/39) after 2 weeks of drainage ($p < 0.02$, $df = 2$). Mean survival time (=no ventriculitis) was 26 days. The probability of drainage without ventriculitis decreased to 0.96 (SE 0.02) after 7 days, 0.86 (SE 0.045) after 14 days, 0.66 (SE 0.1) after 22 days, and 0.53 (SE 1.4) after 26 days. We identified potential risk factors for ventriculitis in eight of 15 patients with ventriculitis, and in nine of 131 patients without ventriculitis ($p < 0.001$, $df = 1$). The risk factors were: leakage in the drainage system (26% with ventriculitis; 8.4% without ventriculitis), disconnection (13.3%; 2.3%), blockage which was cleared by irrigation (20%; 5.3%), and dermal infection (6.6%; 0%).

Comparison of the CSF results in 15 patients who had established ventriculitis with those in 49 patients without ventriculitis showed no significant difference for most of the mentioned indices except the following. Ten of 15 patients with ventriculitis and only eight of 49 patients without ventriculitis showed oligoclonal IgG in the CSF ($p < 0.001$, $df = 1$). Thirteen of 15 patients with ventriculitis and 17 of 49 patients without ventriculitis showed increased CSF lactate (>2.1 mmol/l; $p < 0.001$, $df = 1$).

In all 14 of the 15 patients with microbiologically confirmed ventriculitis available for analysis, maximal lysozyme concentrations of above 2.5 mg/l were found (mean 11.29 (SD 8.1) mg/l, range 2.6-25 mg/l), in 61 samples at different times (figure). In only two of the 31 control patients could lysozyme concentrations just above 2.5 mg/l be detected, with all others lying clearly below this concentration (mean 1.44 (SD 0.64) mg/l, range 0-2.6



Mean concentrations of lysozyme concentration in ventriculitis during the 4 day periods around the detection of bacteria.

mg/l, $p < 0.001$, $df = 1$). In 17 samples, the ventricular concentration of lysozyme was compared with the concentration in lumbar CSF samples taken synchronously. The mean ratio of lumbar to ventricular concentration was 2.24 (SD 0.525) (range 1.4-2.8, 2 tailed $p = 0.0003$, Wilcoxon matched pairs test).

Our study shows a clear connection between the duration of drainage and the risk of ventriculitis. The indication for implanting or continuing ventricular drainage should therefore be checked daily, and alternatives such as catheter exchange should be considered at an early stage. The documented risk factors show that improving the standards of hygiene and nursing care are necessary for reduction of the risk of ventriculitis. We found the presence of oligoclonal IgG bands, CSF IgM,⁵ CSF lactate, and lysozyme in the CSF to be statistically relevant indices for diagnosis. The finding that lysozyme concentrations in lumbar CSF are more than twice as high as in ventricular CSF has not to our knowledge been described previously. Evidently lysozyme, as a relatively large protein molecule, is concentrated in the lumbar CSF. The interpretation and the definition of normal values must take account of these findings.

This study shows that a single, marginally pathological value has less diagnostic value than an increase in lysozyme detected in a series of CSF samples. As a pragmatic approach to early diagnosis of ventriculitis, we recommend a CSF analysis within the 1st week, including measurement of lysozyme concentration. If drainage is to be continued longer than 1 week, we would advise daily CSF analysis, in particular of lysozyme. If there is a relative increase in lysozyme concentration, ventriculitis should be assumed, even when microbiological findings are still negative.

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Clinicoanatomical correlates of a Fourire prodromique in a pontine infarction

Pathological laughter heralding a neurological deficit was first described by Ferré in 1903 as *Fourire prodromique*.^{1,2} We present a patient with prodromal pathological laughter and a right pontine infarction in the territory of the paramedian branch of the basilar artery. These are the first clinicoanatomical correlates integrating MRI lesion mapping with

immunohistochemical studies for a serotonergic specific enzyme of human brain stems.

A right handed 61 year old woman was admitted to hospital for a left hemiplegia. She presented with a history of diabetes, high blood pressure, and an old myocardial infarct. She had experienced spells of uncontrolled and inappropriate laughter during the night and the subsequent morning. At noon, her left side became paralysed. On admission, she was alert, attentive, and had a right sixth nerve palsy and a left hemiparesis that included the face. There was a left Babinski's sign. Neuropsychological testing disclosed a mild attentional deficit and a decreased phonological fluency. There was no lability of affect and no inappropriate crying. She recognised the laughter as abnormal. The spells were usually totally inappropriate and without any associated mirth. Sometimes they could be triggered by an unfamiliar situation, such as talking to the physical therapist. To measure pathological laughter with a validated scale, we used the pathological laughter and crying scale³ (PLCS) and her score was 15/27. A psychiatric evaluation was negative for manic disorder. Brain MRI disclosed an

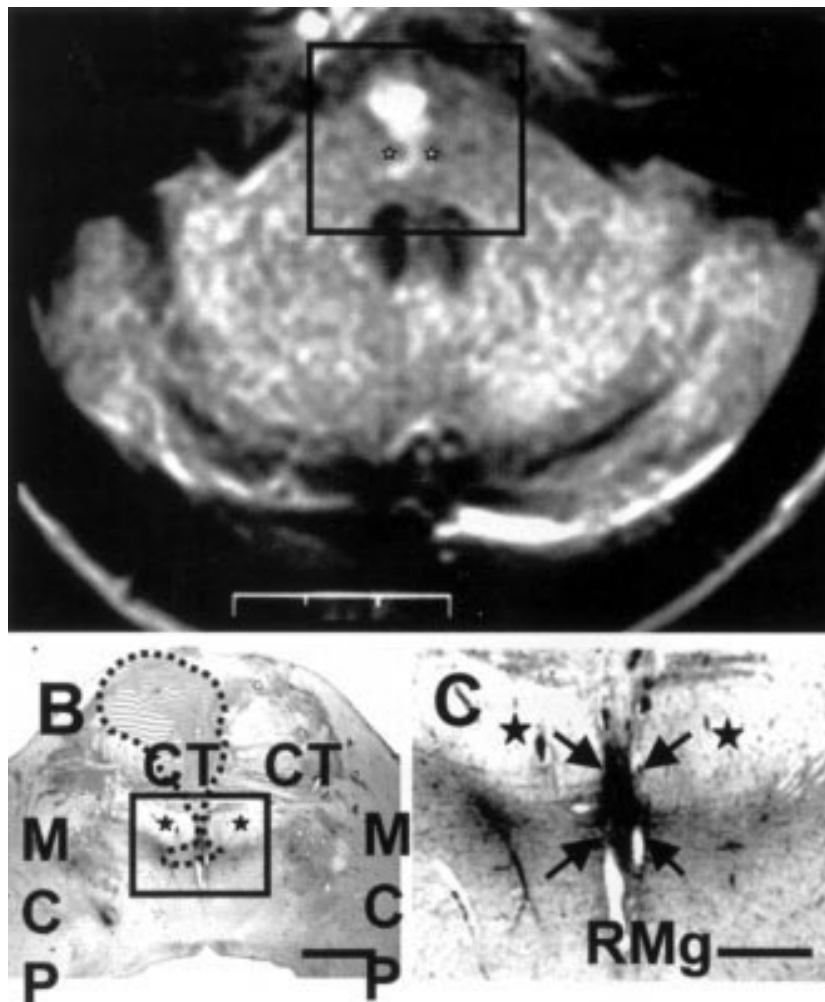
infarction in the right ventral pons without other focal lesion (figure, A). An EEG was normal. Spells of pathological laughter continued for a week then gradually resolved. After 2 weeks, the PLCS score was 2/27.

The limits of the lesion in the right ventral pons were overlaid on a section of a corresponding level taken from a series of immunohistochemical preparations used to map the entire human serotonergic system.⁴ The main tracts and structures involved are shown in the figure (B, C).

Pathological laughter is an exaggerated, uncontrollable, and inappropriate laughter usually unrelated to a true emotion or a congruent mood. It is found in gelastic epilepsy (ictal pathological laughter), associated with lesions in the hypothalamus, anterior cingulate, or basal temporal lobe. Non-ictal pathological laughter is often associated with pathological crying and usually seen with bilateral, multiple cerebral lesions as a component of pseudobulbar palsy. However, non-ictal pathological laughter can occur in patients with unilateral lesion, and without pseudobulbar palsy. In these cases, imaging studies show lesions in the lenticulocapsular, thalamocapsular, and pontine base areas. Recognised causes include strokes or tumours. Non-ictal pathological laughter may also occur in the cortical and subcortical territory of large arteries, usually the middle cerebral artery, and, in these cases, it may be very difficult to distinguish from a gelastic seizure. In prodromal pathological laughter, the locations of the lesions and the pathologies are similar, and include mainly strokes and tumours. The pathophysiology of pathological laughter was discussed by Wilson⁵ in 1924, who suggested a motor release phenomenon. He pointed to an imbalance between voluntary motor pathways in the corticobulbar tract and involuntary pathways from limbic circuits to the facial nerve nucleus, the nucleus ambiguus, and anterior horn cells that subserve the phrenic nerve (faciorespiratory coordination of laughter). Another hypothesis involves serotonergic neurotransmission, originating in the pontine serotonergic raphe nuclei. Pharmacological evidence also shows that serotonin reuptake inhibitors may improve a patient's laughter.³

The raphe nuclei are divided in a rostral and a caudal group.⁴ Nuclei of the rostral group, in the midbrain and rostral pons, project rostrally to the forebrain. They are separated by a gap from the nuclei of the caudal group extending from the caudal pons to the end of the medulla. These nuclei project to the entire brainstem and spinal cord. Serotonergic neurons of the caudal pons lying in the ventral tegmentum belong to the raphe nucleus magnus (RMg), and are at the origin of a widespread innervation of brainstem structures.

Our patient presented with prodromal pathological laughter heralding an infarction in the right ventral pons, in the territory of the paramedian branch of the basilar artery. She had no other signs of pseudobulbar palsy. It is unlikely that pathological laughter in our case was due to seizures (gelastic epilepsy) because of the long duration of the episodes, the absence of altered sensorium, automatisms, or EEG abnormalities, and the location of the stroke. The unique and circumscribed lesion of the corticospinal and corticobulbar tracts at the level of the ventral pons, saving the medial lemniscus, may seem to favour Wilson's hypothesis; however, the posterior angle of the lesion along the midline also



Axial views at the level of the sixth nerve and the middle cerebellar peduncle in the pons. (A) MRI showing the infarct in the right ventral pons. Box area depicted in (B). (B) Micrograph of a human brainstem transverse section at the level corresponding to the MRI, immunostained for a serotonin specific enzyme. The limit of the infarct is overlaid, with respect to the reference structures: (*) = medial lemniscus; CT = corticospinal and corticobulbar tracts; MCP = medial cerebellar peduncles. (C) Enlargement of the boxed area in (B), showing the location of the raphe nucleus magnus (RMg) relative to the medial lemniscus. Scale bars: (A) 1000 µm, (B) 500 µm, (C) 250 µm.

involves the serotonergic RMg (figure, A-C). An involvement of this serotonergic nucleus is further supported by the temporal characteristics of pathological laughter, occurring in transient bursts before the development of motor signs in the limbs. We therefore conjecture that pathological laughter was prodromal because ischaemia began at the distal end of the vascular territory of the paramedian branch of basilar artery involving the RMg first. Both hypotheses could be reconciled if we assume that emotional motor pathways can be modulated by serotonergic neurotransmission from the raphe nuclei. A small lesion involving convergence of both emotional motor pathways and raphe nuclei would also explain the location of prodromal pathological laughter in the pons.

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Proximal median mononeuropathy associated with an anomalous deep course through the brachialis muscle

Proximal median mononeuropathies, unrelated to direct trauma or external compression, are unusual in neurophysiological practice; several syndromes have been more commonly described including the anterior interosseous syndrome, the pronator teres syndrome, and entrapments at the lacertus fibrosus or at the ligament of Struthers.¹

We report the case of a 29 year old woman with an upper median mononeuropathy at an unusual lesional site. She started a new job consisting of repeatedly lifting heavy crates full of apples from the ground, carrying them for a while, and then putting them on a shelf. Fifteen days later, at the end of a working day, she began to complain of right hand weakness with numbness and tingling limited to the first, second, and third fingers; 4 weeks after the onset of symptoms neurological examination showed marked weakness of thumb abduction and opposition, forearm pronation, and flexion of the wrist and of the distal phalanges of the thumb and index finger; she had paraesthesias on the palmar side of the right thumb, index, and middle fingers without spontaneous pain, which could otherwise be strongly evoked by deep palpation of the median nerve trunk at the lower third of the right upper arm. The patient denied any kind of trauma or prolonged direct compression on that limb.

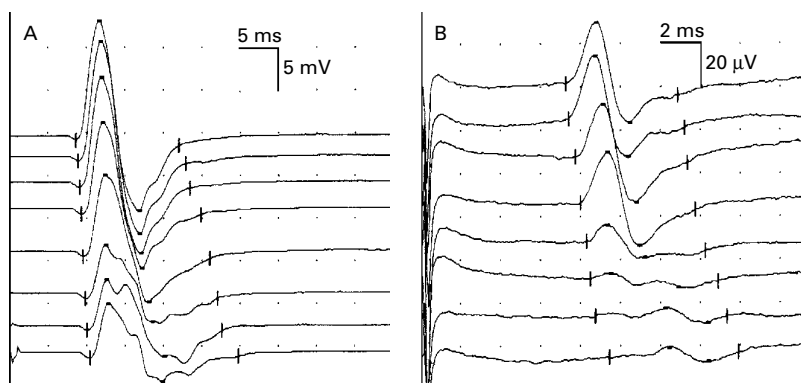


Figure 1 Neurophysiological study: (A) motor and (B) sensory inching of the right median nerve across the site of conduction block; the drop of motor and sensory potentials at latencies 9.8 and 8.3 ms respectively corresponded to a stimulation site located along the nerve course about 9 cm proximal to a line between the biceps tendon and the medial epicondyle; recordings from the abductor brevis pollicis muscle by surface electrodes in (A) and from the third finger by ring electrodes in (B).

Electromyography showed fibrillation potentials and neurogenic motor units recruitment in all forearm right median innervated muscles, including the pronator teres; in thenar median innervated muscles abundant fasciculations and severely reduced recruitment patterns were the major findings, with minimal denervation; on nerve conduction studies the distal right median cMAP had a latency of 4 ms and a positive to negative peak amplitude of 25 mV; antidromic SNAP recorded at the third finger had an onset latency of 3.6 ms and a positive to negative peak amplitude of 70 µV; forearm median motor and sensory conduction velocities were 54 m/s and 60 m/s respectively; stimulation of the median nerve at more proximal sites disclosed a partial motor (fig 1 (A)) and complete sensory (fig 1 (B)) conduction block in the distal third of the upper arm; an inching technique allowed better localisation of the site of conduction block about 9 cm proximal to the elbow along the median nerve course. The rest of the neurophysiological study, performed in four limbs, was normal. Routine blood chemistry was normal, including tests for diabetes, thyroid function, and vasculitis. A study of DNA excluded the presence of the deletion at chromosome 17p11.2-p12.

Radiography of the right humerus ruled out a supracondylar process; an MRI study of the right upper arm using T1 weighted axial images along the nerve course showed the median nerve to be normally recognisable within the arm neurovascular bundle above the lesional site (fig 2 A); following the nerve course in more distal sections the nerve seemed to separate from the bundle as it approached the belly of the brachialis muscle (fig 2 B). In the subsequent more distal sections the nerve was no longer recognisable within the image of the brachialis muscle belly (fig 2 C). At surgical exploration of the right median nerve, the proximal segment seemed to be located within the neurovascular bundle in a deep inferolateral position. At the transition between the middle and the distal third of the arm, where the basilic vein joined the humeral vein, the nerve was found to turn deeply through the brachialis muscle belly from which it emerged about 5 cm more distal. Muscle fibres covering the nerve were sectioned allowing appraisal of a consistent reduction of the size of the nerve throughout its intramuscular course. No other abnor-

malities were detected along the nerve until it entered the antecubital fossa (fig 2 C).

Neurolysis was followed by clinical and neurophysiological improvement. Fifteen days after surgery hand function improved; 2 years later there was no weakness and EMG was consistent with a good reinnervation process.

Our patient presented a subacute upper median mononeuropathy in the distal third of the upper arm associated with an anomalous intramuscular course through the brachialis muscle; this was documented by neurophysiological investigation, imaging studies, and surgical exploration. To our knowledge this is the first report of a median nerve lesion at that site associated with such anatomical findings.

Anatomical variations involving the course or the structure of muscles and nerves and their relations are reported as not uncommon in cadaveric dissection studies of the upper limbs²; as these anatomical variations are rarely associated with peripheral nerve lesions, their pathophysiological relation remains somehow unclear.

For the proximal upper arm Bellmann and Vellander³ described an isolated case of median nerve compression at its origin by an anomalous muscle band originating from the interval between the subscapularis and latissimus dorsi muscles and crossing the neurovascular bundle to reach the anterior surface of the humerus.

In the distal upper arm and elbow region the presence of a supracondylar ligament and the variable relation of the median nerve with the heads of the pronator teres muscle are indeed the most often reported situations predisposing to an entrapment.

A few authors have described even more uncommon anatomical variations at necropsy, discussing their potential role in causing a focal median nerve lesion. Dharap⁴ described a case showing an anomalous muscle arising from the humerus and crossing the median nerve and the brachial artery to blend with the common origin of the forearm flexor muscles. Nakatani *et al*⁵ reported a case in which a muscle slip from an anomalous four headed biceps brachii muscle joined the posterior fascia of the pronator teres forming a tunnel where the median nerve seemed to be compressed.

At the forearm level the median nerve may be compressed by an anomalous palmaris longus muscle or in the hand by anomalous

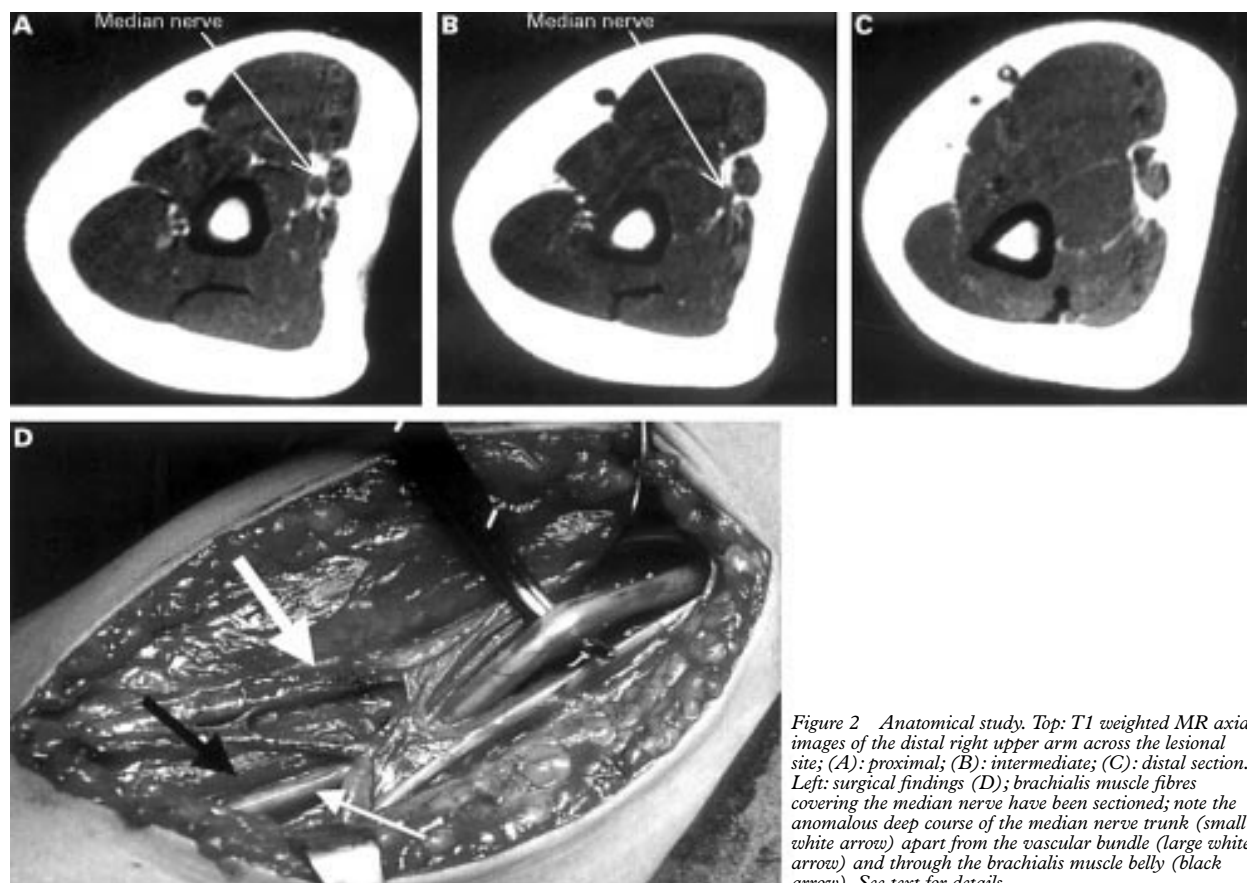


Figure 2 Anatomical study. Top: T1 weighted MR axial images of the distal right upper arm across the lesional site; (A): proximal; (B): intermediate; (C): distal section. Left: surgical findings (D); brachialis muscle fibres covering the median nerve have been sectioned; note the anomalous deep course of the median nerve trunk (small white arrow) apart from the vascular bundle (large white arrow) and through the brachialis muscle belly (black arrow). See text for details.

lumbrical or thenar muscles⁶; similar cases may involve the ulnar and the superficial radial nerves.

The pathophysiology of this type of lesion is mainly mechanical: a repeated and prolonged compression may develop either directly by the contracting muscle itself or by fixation against more rigid osteoligamentous tissues; the movements performed by our patient consisted in repeated and alternated elbow flexions and extensions under loading: in this setting the contracting muscle could also have reduced or blocked the longitudinal sliding of the nerve along its bed, with subsequent stretching and friction of the nerve trunk.⁷

In conclusion, this case emphasises that rare anatomical variations should be considered in the differential diagnosis of proximal median mononeuropathies at uncommon lesional sites.

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Documented growth of a temporal arachnoid cyst

Most arachnoid cysts are probably present at birth, or develop soon after. Once they are formed, they are thought to remain stable, apparently in some kind of equilibrium with the rest of the intracranial space. Not infrequently, cysts have been reported to disappear spontaneously (for references see Wester and Hugdahl¹) and a minority may grow with increasing age, although rather slowly.² Occasionally, cysts in infants have been reported to grow to a substantial size. Kumagai et al.³ reported on a newborn boy who developed a temporal fossa cyst between the age of 2 and 4 months, which later increased considerably before it was removed when the patient was 8 months old.

Except for the very smallest, most arachnoid cysts display radiological signs indicating an increased intracystic or intracranial

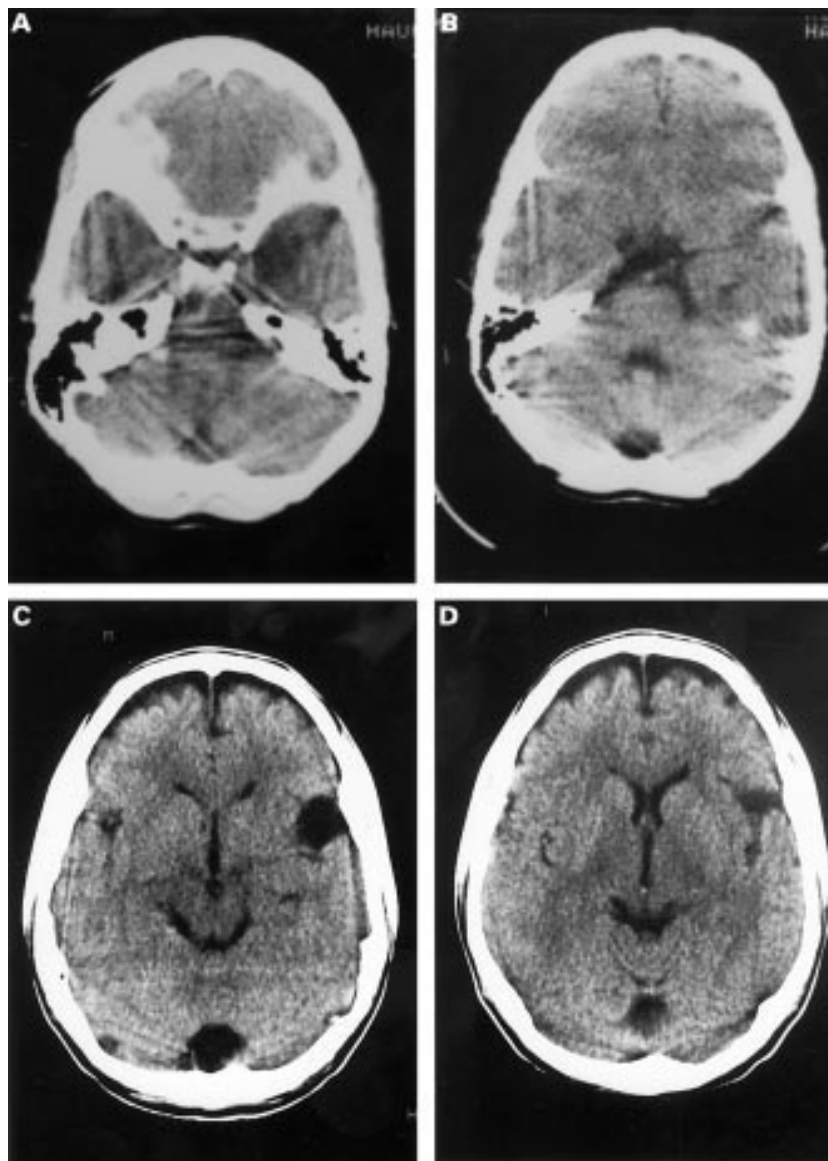
pressure. For example, during infancy and early childhood, cysts may influence the shaping of the adjacent skull bone, in the case of middle fossa cysts resulting in an enlarged fossa, often with a bulging of the overlying bone. Moreover, middle fossa cysts may also dislocate the temporal lobe posteriorly, and larger cysts regularly cause a midline shift, thus indicating expansive forces.

This notion of raised intracystic and intracranial pressures is supported by the common intraoperative finding of a cyst wall bulging out of the dural incision. However, the relative paucity of associated symptoms, the moderate radiological displacement, the absence of perifocal oedema in the adjacent brain parenchyma, and, finally, the total intraoperative impression, all indicate that the pressure is only moderately increased.

It is a common clinical experience that the symptoms caused by an arachnoid cyst may first present after many years, and that the symptoms also may vary over time. Why this is so is not known, but it is tempting to suggest variations in the intracystic pressure as one explanation.

The demonstration of a cyst enlargement over time may be of some importance, as it would provide additional evidence of an increased intracystic pressure, and that arachnoid cysts not merely represent passive accumulations of fluid as implied by the term "the temporal lobe agenesis syndrome".⁴ With the exceptions mentioned above, results from very few patients have been published that show growth of an arachnoid cyst. We hereby report on one such patient.

An 18 year old man had CT at the age of 8 because of complaints thought to be caused by a sinusitis (a moderate transitory headache) and no other symptoms. It was then



(A and B) Axial CT when the patient was 8 years old, showing a small arachnoid cyst in the left middle fossa. (C and D) Axial CT when the patient was 18 years old, showing that the cyst in the left middle fossa had grown considerably, now reaching well above the sphenoidal wing.

discovered that he had a relatively small arachnoid cyst in the left temporal fossa. The cyst did not reach above the sphenoidal wing or the pyramid (figure A and B). As we at that time were not yet aware of the cognitive impairment caused by most temporal cysts,¹ we refrained from surgical decompression.

Ten years later, he was referred to us again, now complaining of a strong, episodic, frontal headache that had developed over the past year. The strength of the headache varied with body position; it increased when he was leaning forward, and was relieved when he was resting on his back. New CT (figure C and D) showed that the cyst had grown considerably. At the age of 8, the cyst volume was 6.5 ml, as calculated from the films. During the next 10 years, the cyst volume nearly tripled, measuring 18.3 ml when he was 18 years of age.

The total intracranial volume was calculated to be 1485 ml on both occasions, with no skull growth occurring between the ages of 8 and 18 years. Also the size of the two middle cranial fossae remained practically

unchanged during the same period. The size of each fossa was calculated from the films, using a standardised technique based on the bony landmarks surrounding it. The right fossa was calculated to contain 19 ml on both occasions, and the somewhat larger left fossa showed a non-insignificant increase, from 24 ml to 24.7 ml.

The patient was operated on under general anaesthesia, with craniotomy, removal of cyst membranes, and fenestration to the basal cisterns. Postoperatively, the left temporal lobe expanded and completely filled the space that had been occupied by the cyst. Thus, the cyst disappeared, and so did his headache. He has now been followed up for 23 months after surgery, without reproduction of the cyst or the headache.

The patient presented here displayed a considerable growth of a temporal arachnoid cyst as seen on two scans 10 years apart. We do not know exactly when the growth took place, but it is tempting to correlate it with the increased symptoms (mainly headache) evolving over the past year before the second CT. In retrospect it is possible, or

even probable, that the patient's headache at the age of 8 also was caused by the cyst, and not a sinusitis. The increase in cystic volume must have occurred after the neurocranium had become relatively rigid, as the patient was already 8 years old before the documented growth started, and the total intracranial volume as well as the volume of the left middle fossa remained constant over the 10 years. Therefore, the cyst growth must have occurred at the expense of brain tissue or the CSF compartment, and cannot be ascribed to a soft, yielding skull allowing an unrestrained growth of the underlying cyst, as we may occasionally see in infants, and as was reported by Kumagai *et al.*³

Thus, the present finding may be taken as an indication that temporal arachnoid cysts are not merely passive accumulations of fluid, and that the cystic growth in this patient must have been caused by an increased intracystic pressure that was sufficient to widen the sylvian fissure, and to dislocate the temporal lobe. In previous studies, it has been shown that this effect on the temporal lobe is sufficient to cause cognitive dysfunction, with postoperative improvement when the cyst is surgically decompressed.¹⁻⁵ In our opinion, such findings alone may constitute a sufficient indication for surgery, but only if the complication rate can be kept at a negligible level.

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Pituitary apoplexy presenting as massive subarachnoid haemorrhage

Pituitary apoplexy is an uncommon, but well recognised clinical syndrome, which usually results from ischaemic or haemorrhagic necrosis of a pituitary adenoma.¹ It is characterised by the abrupt onset of severe headache, visual impairment, ophthalmoplegia and often, a deteriorating level of consciousness.² Signs of meningeal irritation are frequent accompaniments, which may confuse the clinical picture with that of aneurysmal subarachnoid haemorrhage (SAH). We report a case of massive SAH caused by pituitary apoplexy and present the CT and MRI findings.

A 72 year old woman, with nothing in her history to suggest pituitary dysfunction, presented with the abrupt onset of severe headache, vomiting, and gradually deteriorating level of consciousness. A CT examination of the brain without contrast enhancement

showed an extensive basal subarachnoid haemorrhage that had diffused into both sylvian fissures and into the sulci over the convexity of the cerebral hemispheres. In addition there was a rounded heterogeneous density mass in the suprasellar cistern (fig 1 A). After the administration of contrast material the lesion displayed heterogeneous central enhancement (fig 1 B). A ruptured anterior communicating aneurysm was suspected but was excluded by normal cerebral angiography.

Brain MRI confirmed haemorrhage within a pituitary tumour (fig 2 A). It could also be seen that the haemorrhage had ruptured through a defect in the tumour capsule into the subarachnoid space (fig 2 B). Despite the administration of 100 mg hydrocortisone intravenously every 6 hours and cardiopulmonary support her condition progressively worsened and she died 3 days after admission.

The clinical syndrome of pituitary apoplexy evolves within hours to days.² The symptoms vary from mild to severe and can progress rapidly to coma and death. Because many patients are unaware that they harbour a pituitary tumour, pituitary apoplexy is often unrecognised at presentation. In pituitary apoplexy, blood and necrotic tumour tissue are enclosed and compressed within the confined space of the sella turcica, a region that is in close anatomical proximity to the basal cisterns. When the pressure gradient within the sella exceeds the resistance of the surrounding structures, blood is expelled into the subarachnoid space producing a clinical picture that may be indistinguishable from aneurysmal SAH.³ Thus pituitary apoplexy must be included in the differential diagnosis of "angiographically negative" SAH.⁴ Brain CT is the modality of choice in the initial investigation of SAH. It will show the spread and severity of the haemorrhage within the

subarachnoid space, as well as any extension into the brain.¹ When pituitary apoplexy is the cause, CT will usually show the pituitary tumour as well as any recent haemorrhage. Brain MRI is superior to CT in identifying the tumour as well as the associated haemorrhage or infarction. In the case presented here, the enhanced MRI also displayed the defect in the tumour capsule which represented the site of rupture. The management of pituitary apoplexy includes the immediate administration of high dose corticosteroids to combat adrenal insufficiency. When there is rapid deterioration of vision or a progressively worsening level of consciousness, urgent surgery in the form of trans-sphenoidal decompression should be carried out.

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Early detection of non-compliance in Wilson's disease by consecutive copper determination in cerebrospinal fluid

A 41 year old technical employee was diagnosed with Wilson's disease in 1982, 2 years after onset of dysarthria, diplopia, visual deficits, ataxia, and concentration deficits. The patient improved rapidly with *D*-penicillamine and a copper free diet, and has since returned to normal neurological function. Penicillamine was stopped in 1989 and he changed his diet from copper free to a normal diet in 1987. In 1990 he was put on 800 mg zinc a day. During the past 17 years he underwent 20 determinations of copper concentration in CSF for follow up of treatment (figure) as copper concentrations in CSF can be used as an indicator of brain copper concentration in the cerebral manifestation of Wilson's disease.¹⁻⁵

Copper was measured by flameless atomic absorption (Perkin Elmer, HGA 500, Überlingen, Germany). The main resonance line was 324.7 nm with deuterium background compensation and argon as a protective gas; the sample volume was 20 µl using an autosampling system. The CSF was measured undiluted. The patient was now again routinely admitted for monitoring of the efficiency of the treatment. He was free of complaints and the neurological examination as well as a neuropsychological test battery and visually evoked potentials were normal. He explicitly denied any change in diet or drug therapy (zinc, 800 mg a day). We found, however, an almost threefold increase of his CSF copper concentration compared with the previous values (figure). Serum

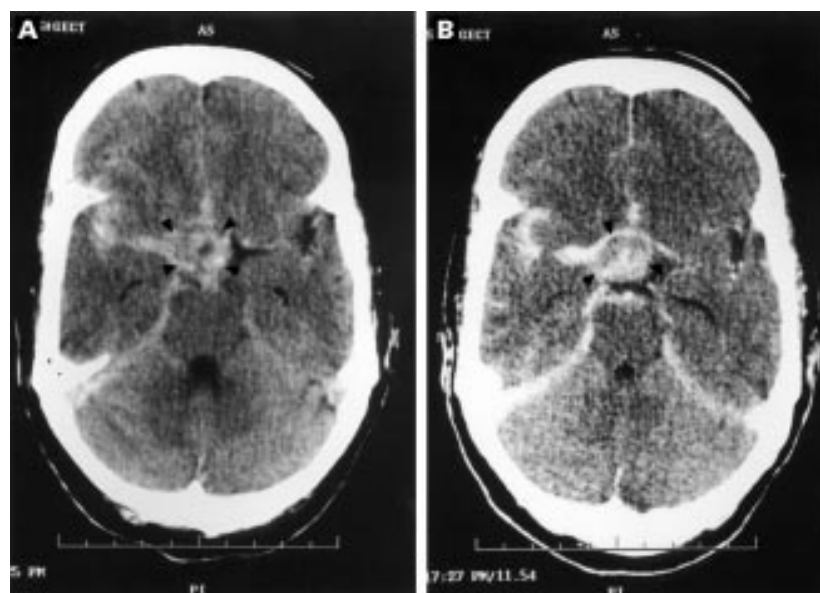


Figure 1 (A) Cranial CT without contrast, showing a heterogeneous but mostly high density mass in the suprasellar cistern (arrowheads). There is also extensive subarachnoid haemorrhage. (B) Cranial CT with contrast, showing central enhancement within a heterogeneous high density mass (arrowheads).

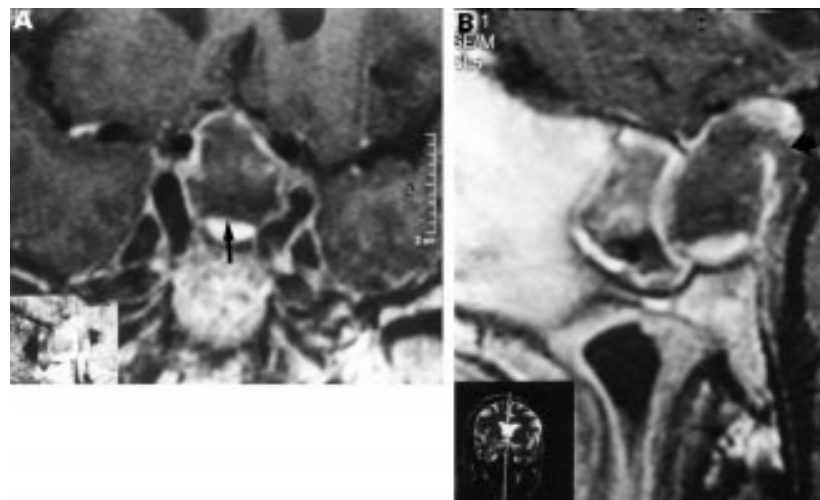
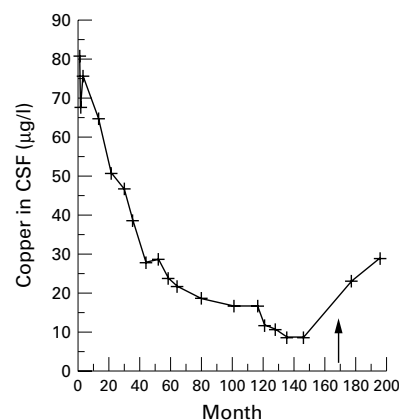


Figure 2 (A) Coronal T1 weighted MRI, showing suprasellar extension of a sellar mass. The area of high intensity signal (arrow) represents methaemoglobin within clotted blood. Note also the hyperintense tumour rim. (B) Contrast enhanced sagittal MRI T1 weighted image, showing that the bulk of the mass is isointense with brain. There is a defect posteriorly in the superior aspect of the capsule representing the site of rupture (arrow).



Copper concentration in CSF during the course of treatment in a 41 year old patient with Wilson's disease. The arrow marks the time when the patient started to take his zinc in reduced doses and irregularly.

copper and ceruloplasmin were unchanged. Confronted with these results the patient admitted that he had been non-adherent to his zinc regimen for the past 2 years by reducing the daily zinc intake to less than 400 mg a day. One established parameter for the efficacy of treatment in Wilson's disease is the balancing of the intake and excretion of copper. This, however, was not feasible as the patient refused to take a standardised diet, rendering the daily copper intake unknown. As is displayed in the figure there had been a continuous decrease of the CSF copper concentrations over the past years, although the treatment consisted only of 800 mg zinc a day without a restriction in copper intake. The repeated determination of the CSF copper allowed for the demonstration of a sufficient treatment and for the detection of non-adherence to the treatment regimen before the reappearance of clinical symptoms. We conclude that the determination of CSF copper reliably detects copper accumulation in the CNS and may be used to monitor the treatment efficacy, particularly in patients with non-adherence to (copper free) diet and drug treatment.

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CORRESPONDENCE

Between will and action

I read with great interest the recent paper by Bundick and Spinella¹ and the related commentary by Goldberg.² These articles address the neurological substrates of volitional disturbance and in places they adopt the vocabulary of the philosophy of action—for example, Goldberg refers to the “will”. However, their uses of action related terms are mutually inconsistent and some clarification might assist in elucidating the functional anatomical relevance of the disorders described.

If we are to use the terms “will” and “action” then their use should be internally consistent. The “will” is that process that deliberates (consciously) on what is to be done, and the “action” is the performance, which follows on from that deliberation.³⁻⁴ (It should be noted that the temporal sequence of this philosophical model of volition is substantially undermined by the classic EEG experiments of Libet *et al* on “intention”.⁵⁻⁶) An “action” is consciously chosen; there is no such thing as an “involuntary action” (according to this model). Involuntary movements are movements not the intended actions of the agent (“the one who acts”).⁴ It follows that the movements initiated by an “alien hand” may seem purposeful, but they are not actions (chosen by the patient). They are failures of action in so far as the patient cannot make the limb “behave”. Hence, although Goldberg refers to the “will” being involved in action generation, his terminology is extrapolated inconsistently: he refers to alien hands performing “purposeful acts” and “involuntary actions”; the first is an attribute of an agent, the second is an oxymoron.⁴

Bundick and Spinella, by contrast, refer to “involuntary motor activity” and “non-purposeful” movements.¹ These terms are coherent within the context of the “will” vocabulary being used.

The above points are not merely pedantic, as a case can be made for “action” and “agency” implicating different brain systems,⁷ and thus the volitional deficit demonstrated in each form of the alien hand syndrome may have some cognitive-neurobiological relevance.

In the medial-prefrontal and callosal forms of alien hand syndrome, the patients, although they have a failure of motor control, and an inability to impose their “will” on the alien limb, do not generally attribute alien agency to that limb—that is, they do not experience it as belonging to an “other”. However, in the posterior alien hand syndrome, personal agency may be lost, and the limb experienced as belonging to someone else. Consider the case of Leiguarda *et al*,⁸ cited by neither Bundick and Spinella nor Goldberg.^{1,2} This alien limb (associated with ictal activity from a right parietal lesion) was experienced thus by the patient:

“Suddenly I had a strange feeling on my left side; later I could not recognize the left arm as my own; I felt it belonged to someone else and wanted to hurt me because it moved towards me.”⁸

This third form of alien hand syndrome has been referred to previously.⁷ The loss of

agency it comprises is consistent with that alienation noted in “somatoparaphrenia” by Critchley⁹ and is congruent with that attribution of agency to external forces so characteristic of schizophrenic “alien control”; itself associated with functional abnormality of the right parietal region.¹⁰

Hence, a consistent application of action terminology may help to elucidate the functional anatomical correlates of disorders of volition.⁷

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Progressive dementia and gait disorder in a 78 year old woman

Although the provisional diagnosis of gliomatosis cerebri in the *clinicopathological case conference* by Tagliati *et al* was the one eventually validated at necropsy,¹ the discussion should also have entertained the possibility that the occurrence of signal hyperintensity on MRI, in the context of dementia, ataxia, and Babinski's sign could also be consistent with the diagnosis of cerebral amyloid angiopathy (with giant cell inflammatory reaction to B4-amyloid and vasculitis), exemplified by a 63 year old man presenting with some of these stigmata.² In the classic triad, consisting of cognitive impairment, upper motor neuron signs, and lobar haemorrhage,³ the third might well be a criterion potentially interchangeable with, or antedated by amyloid related vasculitis and attendant stigmata such as focal non-specific hyperintensity on MRI.

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Guillain-Barré, Fisher, and Bickerstaff syndromes: nature versus well established ideas

As the author of the first ever report documenting central nervous system involvement in Miller Fisher syndrome,¹ I beg permission to discuss certain aspects of the work of Yuki *et al* on Guillain-Barré syndrome and Bickerstaff's brainstem encephalitis, an example of which was published in this *Journal*.² Twenty three years ago, I perused the literature in search of a diagnosis for a child I had seen in Iran. Eyeing incessantly a few certain guide posts in the neurological heavens (Babinski's response, internuclear ophthalmoplegia, spasticity) I sailed the lore diligently, arriving at two inescapable conclusions: (a) that my patient with a midbrain lesion demonstrated by CT was an instance of Miller Fisher syndrome, hitherto a variant of Guillain-Barré syndrome; (b) that Bickerstaff's brainstem encephalitis and Miller Fisher syndrome are one and the same entity. With that perusal behind me, I thought it entirely sufficient to include Bickerstaff's work in my references and ended the article by the following statement: It is evident that our finding, if confirmed, raises questions regarding pathophysiology of Landry-Guillain-Barré syndrome, of which Fisher syndrome is a limited form. That pivotal observation has since been amply substantiated (see below for an incomplete list of references).

In 1982 the article became the subject of an editorial in the *Archives of Neurology* in opposition to my position. It was acknowledged parenthetically by Bickerstaff himself who eventually embraced my second conclusion even though he sided with the splitters, considering the entity of a separate disease. The arrival of MRI turned the tide entirely in favour of the lumpers soon after³, confirming my impression of a need for a reappraisal indicated above. Electrophysiological studies pointed to the same conclusion—that is, Miller Fisher syndrome often, if not always, is superimposed on a Guillain-Barré syndrome background sometimes so mild requiring complex techniques to disclose its presence.⁴ Frequent shuttling of Yuki *et al* between Guillain-Barré syndrome, Bickerstaff's brainstem encephalitis, and Miller Fisher syndrome when reporting "overlapping" hybrid cases means the same thing as well. Many others have made similar observations describing an ascending or descending march of the pathology along the brainstem, displaying corresponding neurological features.⁵ The report of Odaka *et al* concerning ballism⁶ in a case of Guillain-Barré syndrome/Miller Fisher syndrome is a novel observation, and another warning to those remaining sceptics who, while ignoring other guide posts, consider Miller Fisher syndrome strictly a peripheral nervous system disease. But when Yuki *et al* draw any distinction between Fisher and Bickerstaff syndromes they are displaying a lack of historical perspective and paucity of clinical perspicuity which I am rectifying here, as this is an important area of neurology where the stakes are high and simple logic must prevail. It is this blurring of traditional border between certain maladies affecting the peripheral and central nervous system that is the thrust of what has followed our ground breaking observation, including the work of Yuki *et al* (whatever its eventual immunological import may be).

The role of MRI in the ensuing events which sometimes resembled an eponymous war deserves a comment. Whereas Ropper and others mistakenly relied on the absence of a lesion in conventional MRI to refute the role of a central nervous system lesion in Miller Fisher syndrome such instances are more cogently explained as follows: (a) the existence of a pathological difference between a signal producing inflammation and mere presence of a viral infection in the central nervous system; for example, in a recent report 30% of clinically proved enterovirus 71 related rhombencephalitis had negative conventional MRI⁷; (b) the subject of "normal appearing" white matter when in fact it is not normal may one day loom large here as it has in the case of multiple sclerosis.

Thus our novel observation of 1979 alleviated Fisher's "certain reluctance to upset well established ideas concerning the disease (Guillain-Barré syndrome)" and removed the stigma of "oddity" and "aberration" from the syndrome described by the two luminaries, Miller Fisher and Bickerstaff, who did not know of each others' contributions; nor could they have known of the fact that they were describing the same clinical entity. And for two good reasons—that is, sharing the above mentioned reluctance to upset the well established ideas concerning Guillain-Barré syndrome (as admitted by Fisher himself) and preceding the wonderful age of computerised neuroimaging by a quarter of a century. It was left to the serendipitous observation in a 7 year old Persian girl, and its aftermath, for the facts to be gleaned—as depicted here.

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Yuki replies:

Derakhshan wrote "when Yuki *et al* draw any distinction between Fisher and Bickerstaff syndromes they are displaying a lack of historical perspective", but we had described in detail the historical background in the introduction of our original paper,¹ which he did not cite. In 1951, Bickerstaff and Cloake² described three patients who had ophthalmoplegia and ataxia as a grave syndrome they called "mesencephalitis and rhombencephalitis". They speculated that the aetiology of Bickerstaff's brainstem encephalitis is similar to that of Guillain-Barré syndrome because prodromal upper respiratory infection, are-

flexia, and CSF albumino-cytological dissociation were detected. In 1956, Fisher³ described three patients who presented with acute ophthalmoplegia, ataxia of the cerebellar type, and areflexia as a variant of Guillain-Barré syndrome. One of the three patients showed mild drowsiness. In 1957, Bickerstaff⁴ added five more patients to the original study and named the condition "brain-stem encephalitis". In 1982, Al-Din *et al*⁵ (Bickerstaff being one of the authors) described 18 patients, and considered Bickerstaff's brainstem encephalitis to be a distinct clinical entity, not a variant of Guillain-Barré syndrome on the basis of radiological (three patients) and pathological (one patient) changes in the brainstem. In 1983, Ropper,⁶ however, criticised their report. He considered that six of the 18 cases reported by Bickerstaff's group were typical Miller Fisher syndrome, and that the other 12 represented obscure brainstem lesions without peripheral polyneuropathy. In 1987, Al-Din⁵ described two cases in which there was an altered state of consciousness and motor nerve dysfunction, in addition to the triad of Miller Fisher. He presented a "spectrum hypothesis", in which Guillain-Barré syndrome and the syndrome of ophthalmoplegia, ataxia, and areflexia are at opposite ends of a broad spectrum, although clinically and pathologically distinct. He regarded his reported cases as being in the middle of that spectrum.

Patients showing drowsiness, brisk reflexes, extensor plantar responses, and hemisensory disturbance, or central nervous system pleocytosis usually are considered to have Bickerstaff's brainstem encephalitis rather than Miller Fisher syndrome. Opinions differ as to whether these two conditions are distinct or related because the aetiology had yet to be established. While studying serum samples from patients with Miller Fisher syndrome, our attention was brought back to a patient with Bickerstaff's brainstem encephalitis previously treated in our hospital. In addition to acute ophthalmoplegia and cerebellar ataxia, this patient (patient 2 in Yuki *et al*)¹ had abnormal plantar responses and became comatose. These neurological symptoms, however, disappeared 2 months after onset. At that time, we thought that anti-GQ1b antibody testing could be used to differentiate between Bickerstaff's brainstem encephalitis and Miller Fisher syndrome. Unexpectedly, the patient had the anti-GQ1b IgG antibody. Therefore, we investigated whether two other patients with Bickerstaff's brainstem encephalitis had this antibody. All three patients had high anti-GQ1b IgG antibody titres, which decreased with their clinical improvement.¹ As prior infection is frequent in Bickerstaff's brainstem encephalitis, as in Miller Fisher syndrome and Guillain-Barré syndrome, an autoimmune mechanism was suggested in the pathogenesis of Bickerstaff's brainstem encephalitis. The finding that Bickerstaff's brainstem encephalitis and Miller Fisher syndrome share common autoantibodies suggested that the autoimmune mechanism is common to both and that they are not distinct, but closely related conditions. Bickerstaff and Cloake² speculated that the aetiology of Bickerstaff's brainstem encephalitis is similar to that of Guillain-Barré syndrome, but the nosological relation between the two had yet to be clarified because of the lack of pathological findings in overlapping cases. We therefore reported necropsy findings for a patient in whom overlapping Bickerstaff's brainstem encephalitis

and Guillain-Barré syndrome had been diagnosed clinically.⁸

Effective therapy for Bickerstaff's brainstem encephalitis has yet to be established. As shown, Bickerstaff's brainstem encephalitis and Guillain-Barré syndrome are closely related; therefore, steroids should not be used to treat these disorders. Instead, the established treatments—plasmapheresis and intravenous immunoglobulins (IVIg)—should be used. Recent studies^{9,10} provide theoretical evidence that the removal of anti-GQ1b antibodies is reasonable and beneficial. Some patients with Bickerstaff's brainstem encephalitis respond favourably to plasmapheresis and IVIg.^{11,12} We recommend that no steroids, rather IVIg (or plasmapheresis), be used to treat Bickerstaff's brainstem encephalitis. Controlled clinical trials are needed to establish the efficacy of these procedures as therapy for this disease.

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Intravenous immunoglobulin causing reversible posterior leukoencephalopathy syndrome?

Turner and Willis describe a patient with the Miller Fisher syndrome treated with intravenous immunoglobulin (IVIg), who developed transient confusion and reversible blindness.¹ The authors state that the bilateral occipital lobe changes seen on brain MRI were secondary to cerebral infarction. They postulate that this may have occurred as a result of hyperviscosity, although at the time of the event the plasma viscosity was only marginally raised at 1.85 cP (normal range 1.5-1.72 cP). The images seem to show relative sparing of the cortex, which would be

rather unusual if the cause was indeed an arterial infarct as would be expected if the mechanism was hyperviscosity induced thromboembolism.² The authors do not specifically mention that they excluded a cerebral venous sinus thrombosis with appropriate imaging and although the pattern and clinical history would be slightly unusual, this is a possibility that needs to be considered.

We suspect, however, that this patient actually experienced the reversible posterior leukoencephalopathy syndrome (rPLES). This is a syndrome of reversible symptoms comprising any of altered mental function; headaches; visual loss; seizures; and weakness.^{3,4} The syndrome has been described with many underlying conditions^{3,4} and has previously been reported with IVIg use.^{5,6} The patient reported on¹ has many of the clinical and radiological features of rPLES, in particular the MRI changes are predominantly subcortical and the vision recovered well. A repeat MRI in this case would be useful and should show resolution of the abnormalities seen on T2 weighted imaging with little or no corresponding T1 weighted abnormality, showing that the brain had been oedematous rather than infarcted.

Reversible posterior leukoencephalopathy is an important syndromic diagnosis to make as it obviates the need for extensive stroke related investigations and has different implications for prognosis and future management.

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Turner and Willis reply:

We thank Maddison and Lewis for their considered comments. They suggest cerebral venous sinus thrombosis and reversible posterior leukoencephalopathy syndrome (rPLES) as two differential diagnoses for our reported case of IVIg associated with cerebral infarction.¹ Formal magnetic resonance venography was not performed on the patient; however, the major sinuses were patent on conventional MRI and the clinical picture was relatively short lived, making cerebral sinus thrombosis unlikely. The initial MR scan and a follow up scan 11 days later, after clinical improvement, demonstrated high signal changes on T2 and T1 weighted images in both the cortex and subcortical white matter indicative of irreversible cerebral damage,

most probably infarction. rPLES is a rapidly evolving neurological condition characterised by headache, nausea, and vomiting, visual field disturbances, altered mental status, decreased alertness, and seizures.² The leukoencephalopathy syndromes have a heterogeneous aetiology;³ reversible multifocal encephalopathy has been reported with IVIg,³ but as pointed out by Lewis⁴ the commonest association of rPLESs is hypertension. It has been suggested that in PLES, seizures are the causative factor and essential in the pathogenesis.⁵ Our patient had no evidence of epileptic activity or hypertension. Vasogenic oedema is hypothesised as the pathology of rPLES and explains its reversibility⁶ but clinical improvement is also recognised in thromboembolic pathology. The plasma viscosity was not greatly raised in our patient but there may be other contributing factors for IVIg to cause a thromboembolic phenomenon. It has been shown that IVIg preparations contain anticardiolipin and antiphospholipid antibodies, which may have a role in thromboembolism.⁶ The images shown in our paper¹ may not do justice to the radiological evidence but along with the raised plasma viscosity, the absence of hypertension and seizures we consider cerebral infarction the most likely pathology. Whatever the pathophysiology the lesson remains the same that in unwell patients IVIg should be used cautiously.

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Charles Bonnet syndrome: an example of cortical dissociation syndrome affecting vision?

Although Cole's article was published some time ago,¹ it was brought to our attention only recently during the weekly journal review by one of our senior house officers. Myself and my other neurological colleagues are left with little doubt that the symptoms of visual hallucinations experienced by Cole is due to the Charles Bonnet syndrome (CBS).

This syndrome comprises the triad of visual hallucinations, visual sensory deprivation, and preserved cognitive status. The visual hallucinations in CBS may persist on eye closure (unlike the visual hallucinations of hemianopia) and are often complex, vivid, and elaborate consisting of moving and colourful images. In epidemiological studies, two common factors for CBS were visual

sensory deprivation typically affecting the anterior visual pathway (due to cataract or senile macular degeneration) and advanced age (older than 60 years). As the hallucinatory symptoms in CBS occur with preserved insight, these are not true but pseudohallucinations.

The syndrome occurs as a result of the dissociation between visual perception and visual sensory input in psychologically normal aged people. Functional neuroimaging (fMRI) has shown that the hallucinations of colour, faces, textures, and objects in CBS correlate with the cerebral activity in the ventral extrastriate visual cortex whereas the contents of hallucinations reflect the functional specialisation of this region.² In our experience, carbamazepine has been partially effective in suppressing the visual pseudohallucinations of CBS, presumably because it might inhibit the increased ventral extrastriate neuronal activity in patients with CBS that persists between the attacks of hallucinatory symptoms.²

In Cole's case,¹ the occipital infarct in the dominant (left) hemisphere led to the dissociation between the visual sensory input (now limited to the right striate cortex) and the visual perception sense of the dominant extrastriate and the visual association cortex spared by the ischaemic event. Collicular vision ("blindsight") plays no part in the symptoms of visual hallucination. In the light of the recent fMRI data, CBS may be considered as a visual dissociation syndrome similar to the cortical dissociation syndromes well recognised in the Geschwind model of language function. Cole gives one of the finest clinical examples to illustrate this phenomenon. Why CBS should occur with visual sensory deprivation exclusively in elderly people and not in young people is unknown but it might reflect the nature of neural plasticity in the visual cortex as opposed to the other cortical functions.

We were, however, a little surprised that CBS did not feature even once in the otherwise erudite discussion of the case report.² Did Cole and the reviewers of the *Journal* not consider this common diagnostic possibility?

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Corticobasal ganglionic degeneration and/or frontotemporal dementia?

I read with interest the recent paper by Mathuranath *et al*¹ describing two patients with the pathology of corticobasal ganglionic degeneration (CBD), the first presenting with the syndrome of frontotemporal dementia and the second with a mixed picture dominated by progressive aphasia. The concept that CBD may present with clinical features distinct from the "perceptuomotor" syndrome widely recognised as "classic" of the disorder is not new. However, until recently it had generally been thought that these cases represented the minority and thus could be considered "atypical". However, knowledge about this disorder has evolved since our group and others reported the first

large series. I think that in 2000 it is not appropriate to quote our 1994 book chapter² stating that "Frank dementia or language dysfunctions are said to be rare and, if present, are mild, and typically occur late in the course of the disease," as current wisdom. Within 2 years of that book chapter ourselves and others were reporting alternative presentations for this pathology and most recently we have published the clinical-pathological experience of the Canadian Brain Tissue Bank in a paper that was presumably in press at the time that the paper of Mathuranath *et al* was being reviewed.³ In this study we found that of 13 patients proved pathologically to have CBD, nine presented with cognitive or language disturbances, only one failed to show dementia during the course of the illness and only four were diagnosed as having CBD in life. Since that time, a 14th patient has come to necropsy whose presentation was that of primary progressive aphasia.

There have also been patients reported in the literature by ourselves and others with alternative neuropathological disorders presenting with clinical features that were mistaken for the "classic" (but now it seems not the commonest) phenotype of CBD including progressive supranuclear palsy, Pick's disease, motor neuron inclusion body dementia, Alzheimer's disease, and familial frontotemporal dementia due to chromosome 17 mutations.

In summary, clinical and pathological experience at the turn of the century strongly supports the conclusions of Mathuranath *et al*. Clinical phenotypes have not proved to be restricted to specific pathological substrates and several different clinical phenotypes may be caused by the same underlying pathology, probably largely dependent on the anatomical distribution of greatest involvement. Where I mainly take issue with the authors is in their belief, which largely justifies their report, that a clear distinction between CBD and FTD is "currently accepted". The cumulative literature since our 1994 review, most recently culminating in a monograph on a topic,⁴ indicates that CBD is no longer thought of as a predominantly extrapyramidal disorder that is distinct and unrelated to frontotemporal dementia.

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- 1 Mathuranath PS, Xuereb JH, Bak T, et al. Corticobasal ganglionic degeneration and/or frontotemporal dementia? A report of two overlap cases and review of literature. *J Neurol Neurosurg Psychiatry* 2000;68:304-12.
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Diagnostic criteria for corticobasal degeneration

The study of Mathuranath *et al*¹ of corticobasal degeneration (CBD) and its overlap with frontotemporal dementia (FTD) contributes interesting information to a controversial area of neurodegeneration. Unfortunately it also introduces a potentially confusing histopathological diagnostic error. The authors found oligodendroglial inclusions which they

considered to be glial cytoplasmic inclusions and claimed that these, diagnostic hallmark of multiple system atrophy, "have been described in other neurodegenerative diseases, including CBD". This is clearly not the case.

To support their view the authors refer to two papers^{2,3} reporting, among other cytoskeletal abnormalities, tau positive inclusions in oligodendroglial cells. A letter, published earlier in this *Journal*,⁴ but not quoted in the current paper,¹ has also claimed that glial cytoplasmic inclusions are not exclusive to multiple system atrophy. The evidence is now overwhelming that they are. What the authors of this¹ and the other papers²⁻⁴ have described are indeed tau positive oligodendroglial inclusions, but they are not the same as glial cytoplasmic inclusions.⁵ Oligodendroglial inclusions, chiefly coiled bodies, undoubtedly occur in various neurodegenerative diseases, including CBD, but their morphology and molecular pathology are different from those of glial cytoplasmic inclusions. Whereas glial cytoplasmic inclusions immunostain with α -synuclein⁶ and only with unphosphorylated tau antibodies,⁷ the oligodendroglial inclusions seen in CBD and other neurodegenerative diseases are α -synuclein negative and give positive reaction with both phosphorylated and unphosphorylated tau antibodies. This basic difference has been recognised by a new classification of neurodegenerative disorders: CBD is one of the tauopathies, whereas multiple system atrophy is an α -synucleinopathy. Thus glial cytoplasmic inclusions remain the most consistent and reliable diagnostic hallmarks of multiple system atrophy and do not occur in other neurodegenerative diseases.

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Xuereb and Hodges reply

The topic of how to apply the term "glial cytoplasmic inclusions" and their specificity to a particular disorder is clearly controversial and in a state of evolution. We used glial cytoplasmic inclusions in a non-specific way to indicate simply the presence of cytoplasmic inclusions in glial cells. We found these

inclusions in subcortical oligodendrocytes. Glial inclusions were initially described in multiple system atrophy by Papp *et al* in 1989;¹ their paper brought glial cellular pathology in neurodegenerative disease to the attention of neuropathologists. Cytoplasmic inclusions in glial cells have since been reported in various neurodegenerative diseases. The label "glial cytoplasmic inclusions" and the initials "GCIs" used in the general sense cannot, therefore, properly be regarded as pathognomonic of any single disease entity. Indeed, a neuroscientist without neuropathological training could conceivably misdiagnose tissue as coming from a case of multiple system atrophy if that tissue contained oligodendroglial cytoplasmic inclusions (in silver preparations or ubiquitin immunohistochemistry). Our paper does not, we would argue, contain a "histopathological diagnostic error" as suggested by Lantos.

On the other hand, Lantos' criticism that we made no mention of recent discoveries of α -synuclein involvement in the biology of MSA is justified. In the discussion, we should have emphasised the fact that glial cytoplasmic inclusions in multiple systems atrophy, and so far only in multiple systems atrophy, are indeed α -synuclein-positive and phosphorylated tau negative, whereas the opposite is true for the glial cytoplasmic inclusions of CBD and related tauopathies. Lest the future should see α -synuclein positive glial cytoplasmic inclusions identified in some other disease, it is well to emphasise that the diagnosis of multiple systems atrophy depends on the clinical history and distribution pattern of neurodegeneration (which determines the clinical phenotype), and the presence of α -synuclein positive glial cytoplasmic inclusions is valuable confirmatory evidence in this context.

We also appreciate Lang's comments on the paper and are very pleased that the cumulative Canadian experience mirrors the conclusions of our paper in that language and/or other cognitive disturbances are a virtually universal feature of CBD and in many cases may indeed be the mode of presentation as highlighted by the recent paper by Grimes *et al*² which appeared after the submission of our manuscript.

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Assessment and treatment of dizziness

In a recent editorial, Halmagyi and Cremer consider Menière's disease in their discussion of recurrent spontaneous vertigo.¹ Menière's disease is a diagnosis of exclusion. Many conditions may present with the triad of hearing loss, vertigo, and tinnitus, most importantly vestibular schwannomas.² Gadolinium enhanced MRI imaging is the current gold standard for diagnosing vestibular schwannoma and is mandatory before giving somebody the diagnosis of Menière's disease. The

Committee on Hearing and Equilibrium of the American Academy of Otolaryngology—Head and Neck Surgery have set out guidelines for the diagnosis and evaluation of therapy in Menière's disease.³

Audiostereovestibular testing can be useful in Menière's disease. Caloric testing has poor sensitivity and specificity in diagnosing the disease. Electrocochleography and glycerol dehydration testing can be useful in the earlier stages of the disease before the hearing function is irreversibly and severely lost. In Menière's disease, the most common findings on electrocochleography are an increased summating potential to action potential ratio, a widened summating potential/action potential complex, and a disturbed cochlear microphonic potential.⁴

For medical treatment, dietary advice with strict sodium restriction is useful. However, betahistine probably helps more patients with Menière's disease than any other drugs. Labyrinthine sedatives are also helpful in patients who have severe attacks of vertigo.⁵ Surgical treatment of Menière's disease treats only the vertigo. A wide range of operations have been described, from grommet insertion to vestibular nerve section, all of which have had a similar degree of success. These are particularly difficult to compare due to the huge variations in the natural history of the disease.

Assessment and treatment of patients with balance disturbance covers many specialties, who all approach the problem from slightly different angles with different perspectives. It is important to liaise closely with colleagues in associated specialties to optimise the diagnosis and treatment of these patients.

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Halmagyi and Cremer reply:

One cannot help but feel a certain sense of nostalgia reading Coatesworth's textbook description of Menière's disease: if only the real world was like that. We deal with his comments in order.

Menière's disease is a diagnosis of exclusion—It is difficult to conceive what needs to be excluded in a patient who has repeated devastating attacks of acute spontaneous vertigo lasting several hours as well as unilateral tinnitus, aural fullness, and fluctuating hearing loss. When the audiogram shows a unilateral low frequency sensorineural hearing loss, the caloric test shows a canal paresis and the electrocochleogram shows a pathologically large summating potential to action potential ratio¹ the patient has Menière's disease. Menière's disease is a clinical diagnosis supported by laboratory testing. It is no more a diagnosis of exclusion than is multiple sclerosis.

The vestibular schwannoma story—This is a difficult one. Maybe the answer is that if

someone else is paying and the lawyers are watching anyone with any unilateral balance or hearing problem should have a gadolinium enhanced MRI in case they are harbouring what might eventually become a symptomatic intracanalicular vestibular schwannoma ("acoustic neuroma"). If the patient actually does have one, then the problem becomes not so much the dizziness but what to do about the "tumour". Vestibular schwannomas can, very rarely, present with one, at the most two attacks of acute spontaneous vertigo,² just as they can, rarely, present as sudden hearing loss.³ We see about 2500 new patients each year in our balance disorders clinic and in the past 15 years we have seen three patients with acute spontaneous vertigo who had small vestibular schwannomas.

Caloric testing has poor sensitivity and specificity in diagnosing Menière's disease—In part it depends who does it. Technical standards for caloric testing are in general not as rigorously enforced as those for audiological testing. Some factors that can have a profound influence on the quality of the results include: (a) method of recording—DC electro-oculography versus infrared and video methods; (b) method of removing fixation—eye closure versus darkness; (c) method or irrigation—water versus air.³ Caloric testing (or "ENG") is no more specific for any disease than is EMG. It shows the site of lesion not the nature of the lesion. When one is confident in the technical standards of the caloric testing the most helpful finding in the diagnosis of Menière's disease is a fluctuating unilateral vestibular loss—the vestibular equivalent of the classic fluctuating hearing loss.

Electrocochleography (ECOG)—Again, it depends on who does it. An ECOG with extratympanic recording of the responses to clicks alone is generally useless or worse, misleading. A transtympanic recording of the responses to tone bursts can disclose, unequivocally, the presence of endolymphatic hydrops, the pathophysiological basis of Menière's disease.⁴ The test is, as Coatesworth notes, most useful in the early stages before a severe fixed hearing loss due to loss of hair cells.

Surgery for Menière's disease—Vestibular nerve section stops the vertigo attacks without worsening the hearing but might cause chronic vestibular insufficiency.⁵ Intra-tympanic gentamicin is a lot simpler and safer and might be just as good at stopping the vertigo but can worsen the hearing.⁶ Endolymphatic sac surgery? The controversy still rages.^{7,8}

We certainly agree on the need for cooperation between specialties in the management of patients with dizziness. Neurologists need to work with otolaryngologists who have expertise and interest in otology. The neurologists of Leeds should know how lucky they are to have one.

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BOOK REVIEWS

Cranial base surgery. Edited by JAMES T ROBERTSON, HUGH B COAKHAM, and JON H ROBERTSON. (Pp 688, £150.00). London: Churchill Livingstone, 2000. ISBN 0-443-056854.

Cranial Base Surgery is a multiauthored textbook with internationally recognised contributors from Europe and the United States of America. The stated aim of the editors is to collate the experience of skull base surgeons to provide an account of the contemporary management of skull base lesions including surgical techniques and outcome data. However, because of the rarity of some of the lesions, the authors admit that long term data on their outcomes are not yet available, which precludes definitive statements about the best management plans.

The book is divided into four sections dealing initially with presentation and diagnosis and sequentially with the surgical approaches, pathological conditions and finally with adjuvant therapy for cranial base tumours.

The section on general considerations concentrates on neuroimaging, interventional neuroradiology, neurophysiological monitoring, and neuroanaesthesia. The chapter on critical surgical anatomy is excellent and certainly for this reviewer provided a useful revision exercise.

The chapters dealing with surgical approaches to the cranial base will be most useful to those who are in training rather than providing any new information to those who already have an established practice, although it does provide a logical overview of the different approaches.

The mark of a good operative text is whether, when one has read and digested it, one would have the confidence to undertake the procedure. For experienced surgeons the answer would be yes but for those in training the text is not supported by the quality of the illustrations. These are largely black and white and have been executed by different artists, which gives them a non-uniform appearance. The intraoperative photographs are unsatisfactory; for example, a picture of a juvenile nasopharyngeal angiofibroma was unrecognisable.

The third section comprises 13 chapters relating to the individual surgical pathology of tumours and vascular lesions. In these

chapters there is repetition of the material alluded to in the *surgical approaches* section. Despite this the translabellar subfrontal approach was not described either in the *surgical approaches* section or in the chapter on olfactory groove meningiomas.

The chapters on surgical pathology would have benefited from having standard sub-headings which would have simplified access to specific information such as that relating to outcome data. The excellent chapter by Jennetta and Resnick on microvascular decompression would have provided an ideal template for this, and the intraoperative colour photographs in the chapter on the microsurgical treatment of trigeminal neuralgia demonstrates what might have been achieved in the other chapters where such quality photographs were absent. The management algorithms at the end of each chapter of surgical pathology provide a useful adjunct although I note no mention of stereotactic radiosurgery was made in relation to the treatment of trigeminal neuralgia.

Much work and no little suffering has characterised the evolution of the surgical approaches to the skull base. There can be no doubt that on occasion these formidable surgical procedures may have led to as the authors state "unnecessary significant morbidity". It is incumbent upon us to embrace advances which might in the future make our surgical approaches redundant. It is to be hoped that over the next 10-20 years results of carefully undertaken studies comparing outcome and morbidity between surgery and adjuvant therapies will allow us to make definitive decisions as to how best manage patients with skull base tumours. It is to be hoped that future editions of this text (either as a paper text or CD Rom) will reflect these results.

The last chapter is about primary bone disease of the skull base. It is not clear why it is included in the section relating to adjuvant therapy and would have been more appropriate in the section on surgical pathologies.

The book itself is attractive to look at and handle with good quality paper and font.

In summary, this is an excellent text book review of the state of the art of cranial base surgery, largely fulfilling the stated aims of the editors. I would hope that a future edition would include improved illustrations and more editing of the operative procedures.

I would certainly recommend this book to those in training with an interest in skull base surgery and to those already established who wish to have a definitive textbook to delve into occasionally.

NIGEL MENDOZA

EMG Waveforms: Video Companion to Electromyography and Neuromuscular Disorders. Edited by DAVID C PRESTON and BARBARA E SHAPIRO. (Pp 56, £55.00). Published by Butterworth Heinemann, Oxford, 2000. ISBN 0750672293.

This is a well constructed video with plenty of examples of EMG phenomena of interest to the trainee clinical neurophysiologist. Some common and unusual examples are included which provide an opportunity to recognise them, particularly when they can sometimes be difficult to capture and demonstrate in the clinic.

There are only a few minor areas of concern. It would be helpful to know some of the clinical background behind the various

cases presented, which would probably help in the understanding and interpretation of the various abnormalities. On occasion, the EMG pictures seem to be slightly out of focus and future availability in a digital format might be more convenient. The accompanying booklet is essential (related to the authors' textbook, reviewed in an earlier edition of this *Journal*), and is required reading throughout the video. An auditory commentary may have been easier to follow. For future editions, a quiz type session at the end of the video might also be a useful training exercise.

Despite these reservations, this is a good training video and I recommend it.

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Neural transplantation: an introduction.

By WILLIAM J FREED. (Pp 561, £39.95). Published by MIT Press, London, 2000. ISBN 0 262 06208 9.

This book by Bill Freed summarises the field of neural transplantation and as might be expected from this author the approach is somewhat different. Bill Freed was one of the original scientists involved with the early pioneering work on neural transplants especially in the experimental exploration of adrenal medullary transplants in Parkinson's disease. He is not to be confused with the controversial neurosurgeon Curt Freed, the principal investigator of the recent double blinded embryonic nigral grafts trial in Parkinson's disease. This book is written by one who saw the field develop out of its experimental origins into the clinical domain, and as such should be capable of providing the reader with a balanced rationale to neural transplantation. Unfortunately, it fails to do this because it often rambles off into quasiphilosophical topics, which is a shame as it undermines much that could be gleaned from this tome.

The book begins with a preface that sets the tone of the rest of the book, concluding with a rather odd quotation from *The jigsaw man* by Larry Niven. The book then leads through a series of introductory chapters which includes a list of conditions that may be suitable for transplantation. This list rather extraordinarily contains schizophrenia but other more sensible candidates such as motor neuron disease or cerebellar degenerations do not make an appearance at all. Immersed in this early section of the book is chapter 7 which discusses neural transplants in terms of changes in personality. Although this is of interest it is clearly out of place in an introductory book such as this, not least because it confuses in the readers mind the notion of selective grafts for neurodegenerative conditions with the ludicrous head transplants that some have advocated. Thus the book has the potential to lead the uninitiated to think that the ultimate goal of neural transplantation is brain replacement rather than brain repair. The book thereafter returns to a more logical and better balanced approach but sadly detours at the end into dangerous waters once again with a misjudged final concluding chapter.

In summary, the book contains much of interest but presents it in a fashion that makes it difficult to recommend. So for those wanting an introduction to the subject of neural grafting this is not the book to read, because of its eclectic approach. To those familiar with the field, it represents an interesting

diversion, but is deeply irritating in parts and creates a sense of confusion as to where Bill Freed thinks the field is going—a situation at variance with those actively involved in the field.

ROGER BARKER

Current progress in the understanding of secondary brain damage from trauma and ischaemia. Edited by A BAETHMANN *et al.* (Pp 116; £46). Published by Springer Verlag, Wien, 1999. ISBN 3 211 83313 7.

The editors of this short book have drawn together the *Proceedings of the 6th International Symposium on Mechanisms of Secondary Brain Damage including Novel Developments*, which was held in Mals/Sterzing, Italy in February 1998. It takes the form of a supplement for *Acta Neurochirurgica*, which traditionally contributed significantly to the subject.

The topics covered are variable, written by multiple authors from different nations. They address both the experimental and clinical aspects of brain injury in ischaemia, touching on modern concepts. They are organised under the headings of molecular and cellular mechanisms, cerebral ischaemia, and remaining problems in severe head injury. Each chapter provides comprehensive up to date references.

Although clinical issues are touched on, the general theme of the book is promoting novel ideas in experimental brain ischaemia and their potential extrapolation into the clinical field. As such, it is of great interest to those involved in the experimentation of cerebral trauma and ischaemia, and to those clinicians with a very high subspecialty interest in this arena. Although most of the chapters are of high calibre, those addressing mechanisms of secondary mitochondrial failure, molecular signals for glial activation, gene expression, and recovery from cerebral ischaemia and modelling of the ischaemic penumbra I found particularly informative.

PJ KIRKPATRICK

Neuroimaging: Clinical and Physical Principles. Edited by RA ZIMMERMAN, WA GIBBY, and RF CARMODY. (Pp 1642, £124.00). Published by Springer-Verlag, New York, 2000. ISBN 0 387 94963 1.

This large single volume textbook has almost 30 contributors. Many chapters are written by more than one person, but one of the editors has personally contributed almost a third of the text, including the first 11 chapters on “physical principles”: computed tomography (60 pages) and magnetic resonance imaging (350 pages). The remainder of the book is divided into four sections. “Clinical principles: normal anatomy and variants” consists of one chapter on “normal variations of the skull and its contents”, with 95 figures, but not a single skull radiograph or any reference to anomalies of the cerebral vasculature. There are 15 on “brain and skull”, rather heavily weighted towards children, which is perhaps not surprising given that the first editor is one of America’s foremost paediatric neuroradiologists. The five chapters making up the “orbits, paranasal sinuses, and skull base” are distinctly disappointing, at least two probably best skipped over. The second of the seven chapters on “spine” is a rather superfi-

cial review of myelography, which to a European also seems anachronistic (although I am assured that many myelograms are still carried out in the United States for medicolegal reasons, which seems perverse!). The author claims that “in older patients, who generally have considerable cervical spondylosis and thoracic kyphosis, the C1–2 injection technique is preferred”. Leaving aside the agist slur on elderly Americans, many experienced neuroradiologists would firmly reject this.

Curiously, there are no corresponding chapters on sonography or cerebral or spinal angiography, although chapter 23, “Interventional neuroradiology”, is written so as to suggest that the authors thought the latter topics would be covered elsewhere. Bizarrely, however, the chapter on “haemorrhage” in the principles of MRI section, offers “tips” on angiographic diagnosis of intracranial haemorrhage! Chapter division is rather idiosyncratic throughout, so that, for example, inflammatory disease of the spinal cord is dealt with under “brain and skull”, whereas inflammatory spinal column disease comes 500 pages later. There is significant repetition, two contributors illustrating a metopic suture, and Alzheimer’s disease crops up in about half a dozen different places.

In the 1980s, postgraduate students often sought a recommendation for a single volume neuroradiology textbook. Now there is a handful to choose from, and it is difficult to pick a winner: most, like this one, have merits and failings, some to a greater degree. The choice might be guided by the space left on that quasitheoretical “departmental shelf”; at £124 for a very well produced radiology book, “Neuroimaging” is certainly not unduly expensive. Another text, recently published with the same title, was more obviously oriented towards that no man’s land between neuroradiology and neurology which in Europe is usually referred to as “neuroimaging”. This one is very definitely a neuroradiology text: “Neuroimaging and nuclear medicine” is relegated (appropriately, some would say) to the 13 page appendix B, which includes three and a half pages of text on “clinical applications”.

The text is moderately well written, accepting that not all the authors have English as their first language, but the index could have been better. The illustrations are generally of very good quality (although there are some appalling graphics in chapter 14, and the legends of some figures in chapter 19 do not say what conditions they show). My favourite thing is figure 11.95. The caption, which I quote in its entirety, similarly does not draw attention to the specific radiological features, and one can only wonder whether the author is settling some heartfelt score: “This is a coronal CT scan of a thick-skinned 73-year-old retired businessman”!

IS MOSELY

Pediatric Neurosurgery. Edited by M CHOUX, C DI ROCCO, A D HOCKLEY, *et al.* (Pp 875, £170.00). Published by Churchill Livingstone, London, 1999. ISBN 0 4430 5630 7.

In a suitably resourced healthcare system it is no longer acceptable for children to receive neurosurgical care from a surgeon who only occasionally dabbles with “small adults”. Those who provide paediatric neurosurgical care must understand the differences be-

tween the developing nervous system and the degenerating one that our adult colleagues have to deal with. Likewise it is no longer appropriate to add the odd chapter on children onto a predominantly adult textbook. This multiauthor textbook is therefore welcome and should be on the bookshelf of any department where paediatric neurosurgery is carried out.

It is in competition with two other multiauthor textbooks, all unimaginatively called “Pediatric Neurosurgery”. For the next edition I would advise the publishers to create some distance from the other two by spelling the title properly, for the main difference between this book and the others is that it is predominantly European in its authorship and style, whereas the others are almost exclusively North American. All three books are comprehensive and well written by leaders in the field and the differences between them are predominantly of style. The North American books I find a little too businesslike, being the type of books you just want to look things up in. This European book conveys the same information in a more relaxed style which I find informative, entertaining, and more readable than the competition.

I think that an institution performing paediatric neurosurgery should have all three books in the department. An individual practising or planning a career in paediatric neurosurgery should have at least one, the choice being dependent on which style suits that person. Before being asked to review this volume I had already purchased all three. The American books I keep in my office where I can easily consult them for the odd fact or reference. This book stays on our children’s ward where its style encourages all staff to pick it up and enjoyably read about the conditions they are treating.

PETER RICHARDS

Multiple Sclerosis: the Questions You Have—the Answers You Need. Edited by R C KALB. (Pp 614, US\$39.95). Published by Demos Medical, New York, 2000. ISBN 1–888799–43–9.

People with multiple sclerosis feel deprived of information about their condition, a feeling which is most acute just after formal diagnosis and early in the course of the disease. This new edition of the American question and answer book is published within weeks of a similar, but shorter, publication from Robinson *et al* in the United Kingdom.¹

The book, edited by a clinical psychologist, contains chapters written by specialists, including neurologists, physiotherapists and occupational therapists, speech pathologists, psychologists, nurses, financial advisers, employment experts, and lawyers, some of whom are themselves people with multiple sclerosis. It uses team work to formulate and answer hundreds of potential questions and in an information oriented society in which it is often hard to know which information to trust it promises to be ‘trustworthy, factual and honest’.

The problem with such texts is that the individual questions never seem precisely correct for the individual patient and, despite the chapter headings, it is difficult to find any specific question; questions on treatment, for example, appear in the chapters on neurology, treatment, physical therapy,

and sexuality. None the less, it provides reasonable, comprehensive, and factual answers and does not show the bias of many current internet information services. It is North American in style and content and the useful appendix on resources has little relevance outside the continental United States. It provides information for people with multiple sclerosis and would be useful in a multiple sclerosis resource centre in the United Kingdom provided that the people with multiple sclerosis who use it remember the advice from Dr Schapiro in the forward that "it is no substitute for talking with your health professional".

DAVID BATES

1 Robinson I, *et al.* *MS at your fingertips*. London: Class Publishers, 2000.

Hormone Therapy and the Brain: a Clinical Perspective on the Role of Oestrogen. By V W HENDERSON. (Pp 112, £28.00). Published by Parthenon Publishing Group, Carnforth, 2000. ISBN 1-85070-078-8.

The role of sex steroids in neurological disease is a topic of importance in our aging population and very worthy of discussion. This book is set out in chapters focusing on different individual subspecialties, including dementia, vascular disease, and epilepsy, with an initial backdrop of basic science followed by a discussion of clinical studies and observations. The chapters are concise and well illustrated with pathological material, photographs, and bright flow diagrams. They provide an informative introduction to the field, but lack depth of discussion in clinical applications.

Study findings are often summarised in histogram format, but lack confidence inter-

vals, thus limiting the visual interpretation of data. Studies summarised in figures and tables are numerically referenced and thus do not instantly draw the reader to named research groups whose material would be of further interest.

As a clinician the discussion of dementia caught my interest and the argument for detailed controlled trials of oestrogen in Alzheimer's disease seemed most compelling, perhaps reflecting the author's clear interest in this field.

Overall, this is a relatively light read which serves as an excellent introduction to the field, easily accessible to medical students and junior neuroscientists. I think that it would be a worthy addition to the university library, but the text lacks sufficient meatiness to inspire purchase by the individual neurologist.

KIRSTY HARKNESS

Headache and Facial Pain. By F MONGINI. (Pp 292, DEM 228.00). Published by Thieme, Stuttgart, 1999. ISBN 3 13 116541 3.

There exists a wide discrepancy between the excitement of recent advances in the pathophysiology of headache, including the neurovascular hypothesis of migraine, serotonergic receptor pharmacology, and knowledge of the involvement of brainstem structures in head pain, and the often low level of enthusiasm for headache management in the United Kingdom. In this volume Mongini presents a personal view of headache and facial pain aetiology and management which complements other researchers in the field.

The first section concentrates on the importance of facial, cervical, and masticatory muscles in the aetiology of headache

with some excellent anatomical illustrations. Reference is also made to serotonergic mechanisms in migraine but this could have been expanded to include a more current view of the neurovascular hypothesis of migraine and also a discussion of calcium channelopathies in the pathogenesis of migraine.

The second clinical section describes in detail the examination of the muscles of mastication including palpation of trigger points and recognition of bite abnormalities. This section would have benefited from more discussion of the features of secondary headaches, altered intracranial pressure syndromes, the importance of vascular risk factors in migraine assessment, and unusual variants of migraine such as familial hemiplegic migraine. Mongini includes many clear photographs of patients with abnormalities of masticatory muscles and tension related symptoms to illustrate his points.

The chapters on management of headache are based around case discussions, with an emphasis on physical therapy for the cervical and masticatory muscles and on treatment of comorbidity of depression as being paramount to successful therapy. Whereas the recognition of concurrent depression cannot be over emphasised in its importance it would have been useful to include a comments on the stepwise approach to migraine therapy and a guide to the use of triptans. Perhaps the most obvious omission in this section is a discussion of chronic daily headaches with analgesic misuse, probably the most common problem seen in headache clinics.

This book should be used as an adjunct to other headache texts on the market to give the reader an insight into a management strategy for those patients with challenging and unusual headache problems.

N J GIFFIN